

# Archives of Neurology and Psychiatry

VOLUME 30

SEPTEMBER, 1933

NUMBER 3

## FAMILIAL SPASTIC PARALYSIS

REPORT OF THREE CASES IN ONE FAMILY AND OBSERVATION  
AT NECROPSY

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Familial spastic paralysis is characterized clinically by the hereditary or familial occurrence of spastic paralysis, which is the cardinal and constant symptom of the disease; it is sometimes the only symptom. In a disease of this nature, however, it is hardly to be expected that the lesions should be confined exclusively to the pyramidal tracts; other parts may be and often are involved; accordingly, with the spastic paralysis there have been reported other symptoms, such as defective mental development, convulsions, optic atrophy, nystagmus, extra-ocular palsies, tremors, speech disturbances—especially scanning speech—and muscular atrophies.

The disorder is rare; our purpose is to report the occurrence of the disease in three members of a family seen recently in the neurologic clinic of Northwestern University Medical School, to review the literature and to describe in detail the pathologic findings in the oldest of the three patients.

### REPORT OF CASES

*Family History.*—The paternal grandfather, aged 70, has always been "nervous." In the last ten years he has had three "fainting spells," during which he suddenly became unconscious for about five minutes; when he came to, he was well oriented. In one attack he was observed to "jerk all over." A paternal aunt, at the age of 20, had an attack of manic-depressive depression that lasted for two months. The maternal grandfather had been "nervous," oversensitive, overirritable, shiftless and excessively addicted to alcohol. The father had had "fainting spells" from the age of 10 to 15. These came on especially when he was hungry or in poorly ventilated places. During the spells he experienced an increasing sense of physical weakness; "things would get black," and he "would pass out if he couldn't get air"; on one occasion he lost consciousness. The mother is "nervous," "high-strung" and oversensitive, and has a bad temper. The father has always been a steady worker and a good provider; the mother previous to marriage was a teacher of piano. The parents said that they had never had

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Read in part at a meeting of the Chicago Neurological Society, Dec. 18, 1930.

syphilis and Wassermann tests of the blood of both were negative. The family history was otherwise without significance.

The patients were three brothers, the first, second and third children. A brother, aged 2 years, and a sister, aged 9 months, appear to be normal.

CASE 1.—Joseph S., aged 11 years, was born at full term. The labor was normal. The weight at birth was  $5\frac{3}{4}$  pounds (2,607 Gm.). There was neither postnatal asphyxia nor convulsions. The patient took to the breast readily and was breast fed for three months, after which, on the advice of a physician, he was fed by bottle. The parents noted early that he was different from other infants; he was not so active, he did not smile, he cried very little, and he was inert and not so alert. He was always rigid and hard to dress. The first teeth erupted at 11 months; he held the head up at 15 months, sat up alone at 3 years, crawled at 4 years and began to walk at  $7\frac{1}{2}$  years. The gait was always awkward; he walked with the "knees and hips bent and with short steps." As far back as the parents could remember the arms were stiff and awkward. He never talked. He began to have convulsions at the age of 2, and had them thereafter at intervals varying from one a day to one in two weeks. He was incontinent of urine and feces. He had no other diseases. This patient died.

CASE 2.—Glenn S., aged 9 years, was born thirteen months after Joseph. The labor was normal. There were neither postnatal convulsions nor asphyxia. The patient took to the breast readily and was breast fed for fourteen months. As a baby he was quiet, inert and unalert. He was always rigid and hard to dress. He sat up alone at 9 months, crawled at 20 months, and walked first at 5 years. The gait was similar to that of the brother Joseph. The movements of the arms were clumsy. He has never talked. He has always been incontinent of urine and feces. From the age of 7 years he has had convulsions, ranging in frequency from one a day to one a month. There have been no other illnesses.

CASE 3.—Lyle S., aged 8 years, was born by normal labor, without postnatal asphyxia or convulsions. He took to the breast readily and was breast fed for fourteen months. As an infant he smiled and cried very little, was inactive and unalert, and was rigid and hard to dress. He crawled at 18 months and walked at 3 years. The gait was similar to that of the two brothers. The movements of the arms were awkward. He has never talked. Since the age of  $6\frac{1}{2}$  years, he has had convulsions, varying in frequency from one a day to one in two weeks. He has always been incontinent of urine and feces.

*Examination.*—To avoid repetition, the essential objective findings in all three cases will be given together. Since the patients could not understand spoken language, examination had to be limited to maneuvers not dependent on the cooperation of the patients. All three children had spastic paraplegia, with markedly increased tonus and exaggerated deep reflexes. Joseph had bilateral Babinski, Oppenheim, Chaddock and Gordon signs and ankle clonus; Lyle had a Babinski sign on the right and an Oppenheim sign on the left; Glenn had a Babinski sign on the right and Oppenheim and Chaddock signs and ankle clonus on the left. The abdominal and cremasteric reflexes were absent in all three patients. The movements of the upper extremities in the three boys were awkward and clumsy, with reflexes that were from slow to brisk, except that the right arm of Lyle showed definite spastic paralysis with exaggerated reflexes. All three boys had a modified scissors gait, walking with adduction of the thighs, genu valgum and flexion at the knees and hips. Slight equinovarus was present in Lyle. All three had vision, although it was not possible to determine how much; in all the disks were normal; there was no ptosis, strabismus or nystagmus; the pupils reacted

to light. There appeared to be no weakness of the jaws. There were no facial asymmetries. All three boys could hear, but it was not possible to determine how acutely. There were no disturbances of deglutition; the soft palates moved mesially. There were no atrophies, fibrillary twitchings, tremors or choreic or athetoid movements. All three boys seemed to be sensitive to pinprick over all parts. All three were idiots; in all the Wassermann test of the blood was negative.

#### SIMILAR CASES IN THE LITERATURE

Familial spastic paralysis was first described by Seeligmüller,<sup>1</sup> in 1876. In 1916, Rhein<sup>2</sup> reported a case and reviewed all of the published cases up to that time; he found, reported by some ninety observers, 111 families with various forms of familial spastic paralysis. He stated that these cases could be readily divided into various classes. Of the 111 families, 36 presented a pure type of spastic paraplegia. In 7 families the arms were involved. In 7 other families, tremor of the arms and legs was associated with spastic paraplegia. In 20 families, cerebral symptoms occurred. In 6 families, atrophy of the arms or legs complicated the picture. In 6 families, bulbar symptoms were present. In 8 families, a disseminated sclerosis syndrome was present. In 8 families there were symptoms of cerebral diplegia. The disease developed from the walking age up to 70 years. In 72 families, the symptoms began under 18 years of age, and in 46 of these they began under 10 years of age. In some families symptoms appeared in some members who were over 10 years of age and in others who were under 10 years of age. Many cases seemed to follow infectious diseases; some other cases were associated with parental syphilis. Some cases occurred in families showing other neuropathic manifestations. A few of the patients were born of consanguineous parents, but in most cases the family history was without significance. Rhein found that in 22 instances the disease occurred in two generations; in 4 instances, in three generations; in 3 instances, in four generations, and in 1 instance, in five generations.

On the basis of his studies Rhein delimited seven groups: (1) cases in which the legs alone are affected; (2) cases in which the disease extends to the arms and may or may not be associated with some mental failure; (3) cases with symptoms indicating implication of the cerebellum: nystagmus and scanning speech, with or without mental deficiency; (4) cases with bulbar symptoms added to the spasticity, which involves the arms and legs; (5) cases associated with muscular atrophy, in either the legs or the arms; (6) cases with tremor in the legs or the arms or both, with which may also be classified cases in which the symptoms are those or resemble those of disseminated sclerosis; (7) cases of familial spastic diplegia.

1. Seeligmüller, O.: *Deutsche med. Wchnschr.* **3**:185, 1876.

2. Rhein, J. H. W.: *J. Nerv. & Ment. Dis.* **44**:115 (Aug.) 1916.

Since the publication of Rhein's review we have been able to find reports of forty families with this disease.

Riggs<sup>3</sup> reported a case in which the familial history was negative for this disease, except that an uncle on the father's side had epilepsy and there was hemophilia on the mother's side. There were six children, three boys and three girls; only the latter were affected. The age of onset varied from 20 months to 3½ years. The symptoms in this family were spastic paraplegia (in one case diplegia), speech disturbances, muscular atrophies and visual disturbances.

Leitner<sup>4</sup> reported a family in which this disease was found in the father and six brothers, one of whom Leitner examined. The patient examined was 29 years of age; the illness had been of six months' duration; abnormal findings were present in the lower extremities only. The musculature of the legs was rigid; the patellar reflexes were much increased; Babinski, Strümpell and Oppenheim reflexes were present.

Williams<sup>5</sup> described a family in which the disease was present in two brothers and a sister. The ages at onset were 5, 7 and 11 years. The lower extremities were affected in all three; in two there was paresis of the upper extremities; in two, failing vision, and in one, difficulty in swallowing. All three had defective, scanning speech, and all were feeble-minded. Williams traced 250 members of the family and found delinquency, criminality, epilepsy, imbecility, alcoholism, psychoses, neuroses, organic nervous diseases, illegitimacy, tuberculosis and cancer.

Mason and Reinhoff<sup>6</sup> recorded a family in which spastic paralysis occurred in four members in three generations. The age at onset was from 4 to 14 years. All four had spastic paresis of the lower extremities and an intention tremor of the upper extremities; three had speech disturbances, indistinct speech and tremulous voice; one had intention tremor of the tongue, and one was feeble-minded.

Manson<sup>7</sup> found spastic paraplegia in four members of one generation, the two survivors of whom he examined. The onset was at an age between 7 and 8 years in all; in the two patients examined there were, in addition to spastic paraplegia, slow speech, clumsy articulation, lateral nystagmus and mental retardation.

Kretschmer<sup>8</sup> reported the disease in three brothers. The familial history was negative. The members affected were the first three of four children; the fourth, a girl, was not affected. In all three brothers the disease started at the age of 12. The findings were very similar in every instance: spastic paraplegia (tetraplegia in two), clubfeet, partial optic atrophy, dysarthria and mental enfeeblement.

De Stefano<sup>9</sup> reported spastic paralysis in two families. In one, there were four cases in one generation, two of which he observed. The parents were syphilitic. The two observed patients had spastic paresis of the arms and legs, and mental enfeeblement. In the other family the parents were related; the mother presented a positive Wassermann reaction; one sister and two brothers were affected. The age of onset in these children was between 4 and 5 years. In all three there was spastic paresis of the lower extremities, and in one the intelli-

3. Riggs, C. E.: *J. Nerv. & Ment. Dis.* **44**:445, 1917.

4. Leitner, P.: *Wien. klin. Wchnschr.* **30**:1144, 1916.

5. Williams, G. H.: *J. Nerv. & Ment. Dis.* **47**:427, 1918.

6. Mason, V. R., and Reinhoff, W. F.: *Bull. Johns Hopkins Hosp.* **31**:215, 1920.

7. Manson, J. S.: *Brit. M. J.* **2**:477, 1920.

8. Kretschmer, E.: *Deutsche med. Wchnschr.* **16**:1241, 1920.

9. de Stefano, S.: *Pediatrics* **28**:895, 1920.

gence was dull. All three patients gave a positive Wassermann reaction with the blood; one had Hutchinson's teeth.

Grünwald<sup>10</sup> found the disease in eight members of four generations; in a ninth member, in the fifth generation, its presence was questionable. The father's family history was of no significance; all cases were in the male members of the mother's family. Grünwald examined two patients. The developmental histories of these two were normal; the age at onset was 4 years in one and 5 years in the other; both presented a picture of pure spastic paraplegia; the symptoms were confined to the legs.

Donini<sup>11</sup> reported the disease in two brothers with a negative family history. In one, the disease began at 13 years; in the other, at 14 years. In one there was complete sacralization of the fifth lumbar vertebra with slight kyphosis of the last three dorsal and first two lumbar vertebrae. One of the patients and two healthy brothers stammered.

Van Gehuchten<sup>12</sup> described a family in which spastic paraplegia alone occurred in the mother and four children; the age at onset in the mother was 35 years; in the children, between 28 and 30 years. A brother, a sister and a nephew of the mother were similarly affected.

Mingazzini<sup>13</sup> described the disease in two brothers and a sister on a heredo-syphilitic basis. The father was tabetic. The three siblings at puberty began to suffer from progressive motor disturbances of the lower extremities, terminating in the syndrome of familial spastic paralysis. One of the brothers had optic atrophy, choroiditis and double cataract. All three were feeble-minded.

Wolpert<sup>14</sup> described the cases of three brothers, aged 23, 19 and 17½ years, in whom spastic paresis of the lower extremities, atrophy of the temporal halves of the disks and intelligence defects gradually developed in late childhood.

Moore<sup>15</sup> described a family in which the father began to lose vision at 40; a paternal uncle began to have a reeling gait at 40; a paternal aunt had a reeling gait. The patient, aged 21 when seen, had had a reeling gait since 14 and gradual loss of vision since 15. Superficial and deep reflexes were increased; there were a bilateral Babinski sign and at times ankle and patellar clonus. The mentality was normal.

Schaffer<sup>16</sup> described the disease in two brothers, aged 28 and 37. In both the onset occurred at 3 years; in both all extremities were involved, but the upper not so much as the lower; both had speech disturbances, and nystagmus when looking markedly to the side. The mentality was normal. The maternal and paternal grandfathers were brothers. The father died at 61; he was demented toward the last.

Roger and Smadja<sup>17</sup> reported a family in which the father was syphilitic. Two female children, aged 10 and 9, became afflicted with spastic paralysis at the age of 5. In both sisters all four extremities were involved; the older was

10. Grünwald, E. A.: *J. f. Psychol. u. Neurol.* **26**:112, 1920.

11. Donini, G.: *Gior. di clin. med.* **1**:401, 1920.

12. van Gehuchten, P.: *Rev. neurol.* **27**:901, 1920.

13. Mingazzini, D.: *Family Spastic Paralysis of Spinal Type on a Heredo-syphilitic Basis*, *Arch. Neurol. & Psychiat.* **5**:637 (June) 1921.

14. Wolpert, J.: *Zentralbl. f. d. ges. Neurol. u. Psychiat.* **30**:121, 1922.

15. Moore, J. W.: *Kentucky M. J.* **20**:25, 1922.

16. Schaffer, K.: *Deutsche Ztschr. f. Nerven.* **73**:101, 1922.

17. Roger, H., and Smadja: *Bull. et mém. Soc. méd. d. hôp. de Paris* **46**:72, 1922.

dysarthritic; the younger, dysphagic. Both patients were born prematurely and had signs of hereditary syphilis.

Bremer<sup>18</sup> reported two families. In one there occurred, in six generations, nine females and seven males with hereditary spastic spinal paralysis, of whom Bremer saw nine. The onsets occurred in early childhood or early youth. In the other family there were nine cases in two generations; Bremer saw two of the patients; in this family there were symptoms resembling amyotrophic lateral sclerosis; i. e., in some members there was atrophy of the small muscles of the hand and of the muscles of the arm.

Higier<sup>19</sup> reported the disease in two siblings, based on hereditary syphilis. The father had syphilis. When examined, he showed spastic parietic gait, stuttering and defective intelligence; the Wassermann reaction of his blood was three plus. The oldest child, aged 12, for one year had spastic paresis of the lower extremities. Diminished vision, bilateral optic atrophy, clumsiness and increased reflexes of the upper extremity, defective intelligence and positive Wassermann reaction of the blood were found. The younger, aged 10, had become afflicted three months before. On examination he showed a spastic parietic gait, pallor of both optic disks, nasal speech, awkward movements of the fingers and a positive Wassermann reaction of the blood.

Marfan<sup>20</sup> reported the occurrence of spastic paraplegia on a syphilitic basis in a father and a daughter, aged 10½ years.

Marinesco, Draganesco and Stoicesco<sup>21</sup> reported an interesting family in which, in addition to spastic paralysis, extrapyramidal symptoms were present. The cases were the first of this description to be reported. They occurred in a brother and a sister. Both patients were subject to attacks of generalized hypertonicity. In the brother these attacks were accompanied by conjugate deviation of the eyes, by increase in the pulse rate, the respiratory rate and the arterial tension, and by exaggeration of the oculocardiac reflex, hyperhidrosis and suppression of saliva. On rare occasions, the sister showed conjugate deviation of the eyes.

Specht<sup>22</sup> found 11 cases in three generations—five in males and six in females. The ages at onset varied from 20 to 52 years. He examined five of the patients. In all, the arms and legs were involved, the former much less than the latter. Disturbances of the bladder were present in two and sensory disturbances in one; four could protrude the tongue not at all or very little beyond the teeth.

Ackerman<sup>23</sup> reported a family in which the disease occurred in the mother and two daughters. The onset in the former was at 62; in the latter at 37 and 43. In all three there was spastic paresis of the legs; in one daughter the arms were involved. In the daughters the disease was aggravated by the menopause and infectious diseases (pneumonia and grip).

Cassinis<sup>24</sup> reported the cases of two brothers and a sister. The family history was negative. One brother, who died at 30 years, had had paralysis and contractures of the lower extremities since the age of 3. One brother and the sister were examined by Cassinis. The onset in the sister was at 40; all extremities were involved; there were facial asymmetry, slight lateral nystagmus and mental

18. Bremer, F. W.: *Arch. f. Psychiat. u. Nerven.* **66**:477, 1922.

19. Higier, H.: *Ztschr. f. d. ges. Neurol. u. Psychiat.* **90**:176, 1924.

20. Marfan, A. B.: *Arch. de méd. d. enf.* **97**:1253, 1924.

21. Marinesco, G.; Draganesco, S., and Stoicesco: *Rev. neurol.* **32**:1003, 1925.

22. Specht, R.: *Ztschr. f. d. ges. Neurol. u. Psychiat.* **99**:32, 1925.

23. Ackerman, R.: *Deutsche Ztschr. f. Nerven.* **90**:210, 1926.

24. Cassinis, F.: *Riv. di pat. nerv.* **32**:113, 1927.

deficiency. In the brother the disease started at 18; only the legs were affected. His speech was disturbed, and he was feeble-minded.

Guillain, Alajouanine and Peron<sup>25</sup> reported the cases of two brothers in whom, between the ages of 12 and 13, a condition developed characterized by paraplegia with flexion contracture of the lower extremities, speech disturbances and mental enfeeblement.

Herz<sup>26</sup> described the cases of two siblings who from very early infancy showed progressive cerebral diplegia, with congenital cataract and optic atrophy.

Tonietti<sup>27</sup> reported a family in which the father was born of consanguineous parents and married a first cousin. Two male children were affected. One brother developed normally until 5 years, when spastic weakness in the legs began and became progressively worse. He was backward in school; the speech was slow and nasal. The face was unexpressive, its lines fixed and rigid; the arms were not involved. Another brother died at 11 years with an analogous syndrome.

Eickhoff<sup>28</sup> reported cases in which the family history was negative. Two brothers and two sisters were affected at 18 years with spastic paresis of the legs. All four were feeble-minded. Another sister, who died at the age of 26, had not been able to walk since the age of 17.

Futer<sup>29</sup> reported a family in which four cases occurred in one generation of ten siblings. The family history was negative. The ages at onset were from 9 to 15 years.

Zipperlin<sup>30</sup> observed fourteen cases in four generations. In the first generation the age of onset was not known; in the second generation it occurred in the forties; in the third generation at puberty, and in the fourth, in early childhood. In another family described by Zipperlin the mother was affected at the age of 30 and a daughter at the age of 5.

Powdermaker<sup>31</sup> reported the cases of three brothers with spastic diplegia; all were affected from birth. All three were idiots.

Klein<sup>32</sup> described the disease in a mother and two daughters. In the mother the disease began at the age of 28; in the daughters, at the age of 21.

Stiefler<sup>33</sup> reported three instances of familial "Little's disease." In two families syphilis was found; in the third there was no syphilis, but the patients, twins, were both premature infants.

Fillie<sup>34</sup> reported a family in which the disease was found in the mother and two children. In one child evidences of the disorder were present from birth.

Guerrini<sup>35</sup> found this disorder in three sisters, in all of whom the disease began at the age of about 1½ years. All three showed defective mental development. The family history was negative.

25. Guillain, G.; Alajouanine, T., and Peron, N.: *Rev. neurol.* **1**:289, 1927.

26. Herz, O.: *Monatschr. f. Kinderh.* **37**:135, 1928.

27. Tonietti, F.: *Policlinico (sez. prat.)* **34**:636, 1927.

28. Eickhoff, C.: *Monatschr. f. Psychiat. u. Neurol.* **69**:1, 1928.

29. Futer, D.: *Ztschr. f. d. ges. Neurol. u. Psychiat.* **118**:722, 1929.

30. Zipperlin, E.: *Ztschr. f. d. ges. Neurol. u. Psychiat.* **122**:560, 1929.

31. Powdermaker, F.: *Familial Congenital Spastic Diplegia*, *Am. J. Dis. Child.* **39**:148 (Jan.) 1930.

32. Klein, R.: *Monatschr. f. Psychiat. u. Neurol.* **72**:24, 1929.

33. Stiefler, G.: *J. f. Psychol. u. Neurol.* **37**:362, 1928.

34. Fillie: *Med. Klin.* **25**:1066, 1929.

35. Guerrini, F. Z.: *Arch. argent. de neurol.* **6**:45 (April-May) 1930.

Signa<sup>36</sup> reported three brothers in whom spastic paraplegia had been present since early childhood. There were no other symptoms in these children. The father had had spastic weakness of the legs since early childhood.

Piatnitzky<sup>37</sup> reported spastic paralysis in a father and three daughters. In the latter the symptoms appeared in all at about the age of 3. A paternal uncle was also afflicted with spastic paralysis.

Govseff and Rossin<sup>38</sup> reported spastic paralysis confined to the lower extremities in three siblings, commencing at from 7 to 13 months. In one the disorder appeared after a trauma to the head; in the other two, after infectious diseases. The family history was negative.

The symptoms of familial spastic paralysis usually begin after the age of walking. Our case is unusual in that the disorder was present from birth. Cases in which the disorder was present from birth have been reported by Hagenbach-Burckhardt,<sup>39</sup> Freud,<sup>40</sup> Brower,<sup>41</sup> Batten and Wilkinson,<sup>42</sup> Krafft-Ebing,<sup>43</sup> Herz,<sup>26</sup> Powdermaker,<sup>31</sup> Stiefler<sup>33</sup> (three cases) and Fillie.<sup>34</sup> As far as we can determine, ours is the twelfth case in which the symptoms were present from birth.

Adding the data obtained from a review of the literature since the appearance of Rhein's review to the data given in Rhein's review and including our case, it may be stated that familial spastic paralysis has been described in 152 families. The disease was found in two generations in 32 instances, in three generations in 6 instances, in four generations in 5 instances, in five generations in 1 instance, and in six generations in 1 instance.

#### REPORT OF NECROPSY

*Macroscopic Observations.*—The eldest patient (case 1) died on the evening of July 7, 1930, and a necropsy was done on the morning of July 8, 1930. Considerable difficulty was encountered in detaching the dura from the cranial surfaces, because an almost bonelike union existed between the dura and the cranium. The brain and spinal cord were removed and placed in commercial formaldehyde, 10 per cent, in a physiologic solution of sodium chloride to prevent cellular swelling.

The dura removed from the posterior aspect of the convexity of the brain was thin and almost pure white. There were practically no vascular markings, except a few at the frontal and temporal lobes. The dura was firm. The cerebral and cerebellar hemispheres were symmetrical but smaller than normal. The pia-arachnoid was normally translucent and could be stripped off easily, except on either side of the temporal and frontal lobes.

There was a complete absence of sulci and convolutions over the parietal and occipital lobes (agyria), except at the tips of the latter. No meningeal blood ves-

36. Signa, A.: *Cultura med. mod.* **9**:799 (Oct.) 1930.

37. Piatnitzky, N. N.: *Klin. Med.* **9**:566, 1931.

38. Govseff, N. A., and Rossin, S. A.: *Klin. Med.* **9**:563, 1931.

39. Hagenbach-Burckhardt, E.: *Zentralbl. f. Kinderh.* **13**:89, 1908.

40. Freud, S.: *Neurol. Centralbl.* **22**:512, 1893.

41. Brower, D. P.: *Medicine* **3**:23, 1897.

42. Batten, F. E., and Wilkinson, D.: *Brain* **26**:341, 1914.

43. Krafft-Ebing, E.: *Deutsche Ztschr. f. Nervenhe.* **17**:87, 1900.

sels were seen in these regions. At the tips of the occipital lobes over the convex surfaces, especially on the left side, there were shallow and superficial indications of sulci and convolutions. There was one definite sulcus on either side of the poles of the occipital lobes. The sulci on the inner surface were well developed. There were sulci and gyri in the frontal and temporal lobes. Many of the convolutions here were definitely larger (pachygyria) than normal. This was true particularly of the gyri on the convexity of the brain.

The entire brain was yellowish white and was of a firmer consistency than normal. No macroscopic changes were seen in the cerebellum, pons, medulla and upper cervical cord. The left half of the cerebrum was prepared for special stains



Fig. 1.—Lateral view of the formaldehyde-fixed brain, showing the smallness, the complete absence of sulci and the convolutions over the parietal and occipital lobes (agyria) and pachygyria in the frontal and temporal lobes.

and all the routine stains. The right half was used for photography and myelin sheath preparations of large coronal sections.

The falx cerebri was similar to the dura in color and consistency, but its vascular markings were more numerous. The medial surfaces of each cerebral hemisphere revealed many sulci and gyri, which were almost normal in appearance.

Macroscopically, coronal sections, 1 cm. thick, revealed an apparently normal gray matter with a decrease in the size of the white matter, especially in the occipital and parietal lobes. Along the border between the gray and the white matter there appeared an irregular continuous reddish-brown zone of from 3 to 10 mm. in thickness. In the white matter of the frontal lobe areas there were many round

or oval brown islands. The ventricular system, corpus callosum and the basal ganglia appeared normal.

The entire spinal cord showed no gross abnormalities.

*Microscopic Observations.*—The dura of the brain showed very few vessels. The cyto-architectonics of the various cortices will be described later. Herxheimer scarlet-red stain revealed an excessive amount of fat occupying about two-thirds of the cytoplasm of all the ganglion cells of the entire cerebral cortex. The nucleus was eccentrically placed and appeared normal. Small droplets of fat were seen outside of the glial membrane of the large vessels. Connective tissue stains failed to show evidence of proliferation of connective tissue either in the pia-arachnoid or in the adventitia of the vessels. Cajal gold sublimate, Holzer and nuclear stains did not show abnormal increase in glia nuclei and fibers.

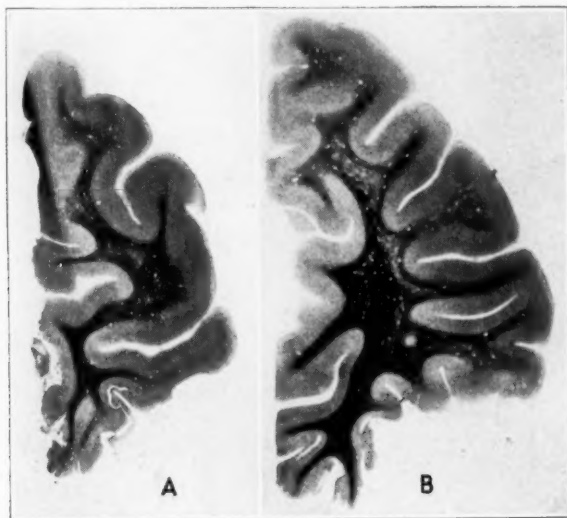


Fig. 2.—*A*, the coronal section through the tip of the frontal lobe showing the large and small gyri with islands of gray substance in the white matter. (Weil stain; photograph.) See figure 12. *B*, the coronal section through the middle of the frontal lobe (right) showing the same gyri as figure 2*A*. (Weil stain; photograph.) See figure 12.

Selected coronal sections of the right half of the brain from the tip of the frontal lobe to the tip of the occipital lobe were stained for myelin sheaths (Weil).

(a) Myelinization: A coronal section (fig. 2*A*) through the tip of the frontal lobe showed large and small gyri, with islands of gray substance in the white matter. With the exception of these islands, the section was practically normal in shape and extent; under a high magnification the white matter showed well myelinated fibers.

A coronal section (fig. 2*B*) through approximately the middle of the frontal lobe showed normal gyri, but an increase of the numerous small unstained areas of the white matter. Most of these islands were situated close to the "U" fibers, which separated them from the gray matter. The callosal fibers stained a deep blue, while the association fibers in the gyri stained a light blue and were poorly defined.

A coronal section (fig. 3*A*) through the knee of the corpus callosum, in contrast with the preceding section, showed that the number of larger gyri (pachygyria) were increased. The unstained areas were concentrated close to the "U" fibers, and no unmyelinated areas were seen in the well stained corona radiata and corpus callosum. The first and third frontal convolutions were pachygyric, while the temporal gyri were normal. The taenia tecta was not seen.

A coronal section (fig. 3*B*) through the head of the caudate nucleus showed absence of gyri on the convex surface of the frontal lobe. The sylvian fissure and the precentral sulcus were well developed. The unmyelinated areas had increased in size, and the "U" fibers which separated them from the gray matter

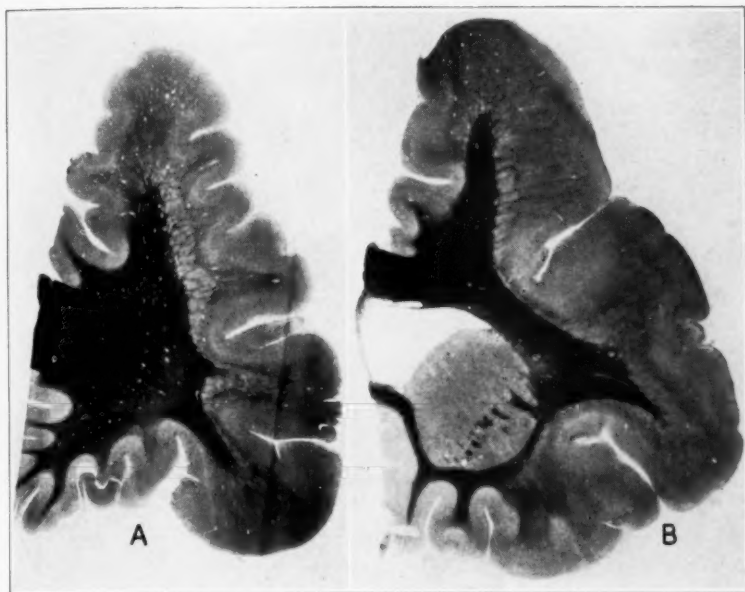


Fig. 3.—*A*, the coronal section through the knee of the corpus callosum showing marked pachygyria with poor myelination and gray islands in the white matter. (Weil stain; photograph.) See figure 12. *B*, the coronal section through the head of the caudate nucleus showing clearly the absence of white matter extending into the cortex. Note the normal basal ganglia and the internal capsule, pachygyria and misplaced islands of gray substance. See figure 12. (Weil stain; photograph.) See text for description.

had disappeared. The caudate nucleus showed a normal myelin picture. The corpus callosum and the corona radiata were well myelinated.

A coronal section (fig. 4*A*) somewhat behind the mamillary bodies showed the neostriatum and paleostriatum, thalamus, body of Luys and part of the mid-brain. There were no sulci on the convex surface of brain, except two shallow sulci at the posterior division of the sylvian fissure. The temporal lobe was fully developed. The unmyelinated areas were markedly increased. The corpus callosum, corona radiata and internal and external capsules were normally myelinated. In the upper part of this section the taenia tecta, the tangential fibers, the frontal gyri, the operculum, the claustrum and the island of Reil were absent. The mark-

ings in the caudate, lenticular and thalamic nuclei and in the structures of the midbrain were normal. On the outer aspect of the corona radiata there were unstained areas.

In a coronal section (fig. 4 *B*) including the limbic convolution, the corpus callosum, the pulvinar of the thalamus, the parietal and temporal lobes, the cornu ammonis and the posterior part of the sylvian fissure, the white matter was reduced to a small strip adjacent to the ventricles. There were four shallow sulci on the convex surface of the temporal lobe. The parietal convolutions formed one large gyrus. The limbic convolution was the only one on the medial surface of this section. The paracentral lobule, the ascending and second parietal, as well



Fig. 4.—*A*, the coronal section behind the mamillary bodies showing the neostriatum and the paleostriatum, the thalamus and the body of Luys. The section shows agyria in the parietal lobe except for its posterior surface above the temporal lobe, and pachygyria in the temporal lobe. Note the myelinization of the white matter in the temporal lobe and the misplaced gray islands. No claustrum or island of Reil can be seen. See text. (Weil stain; photograph.) See figure 12. *B*, the coronal section through the pulvinar and the cornu ammonis, showing the white matter reduced to a narrow strip, misplaced gray islands in the white matter and in the ependyma of the lateral ventricle. Note the pachygyria and agyria. (Weil stain; photograph.) See text and figure 12.

as the first, second and third temporal convolutions, were not seen. The posterior Rolandic sulcus, as well as the internal parietal sulcus, were not represented. The collateral sulcus of the temporal lobe was not represented. The lingual lobule, the corpus callosum, the hippocampus, cornu ammonis, the hippocampal sulcus, the superficial medullary laminae, the subiculum diverticulum and the posterior part

of the trigon were well myelinated. The optic radiations of Gratiolet, the inferior longitudinal fasciculus and the tapetum were fairly well differentiated. The external medullary lamina of the thalamus and the reticular zone were clearly seen. The external capsule was not represented, but the lenticular segment of the internal capsule was seen. Circular and oval nonstaining areas were seen on the outer aspect about the corona radiata of the parietal lobe and about the fasciculus of Türck of the temporal lobe. Unmyelinated areas were present in the parietal and temporal lobes.

In a coronal section (fig. 5 *A*) including the splenium of the corpus callosum, the corona radiata and the posterior horn of the lateral ventricle, the myelinated

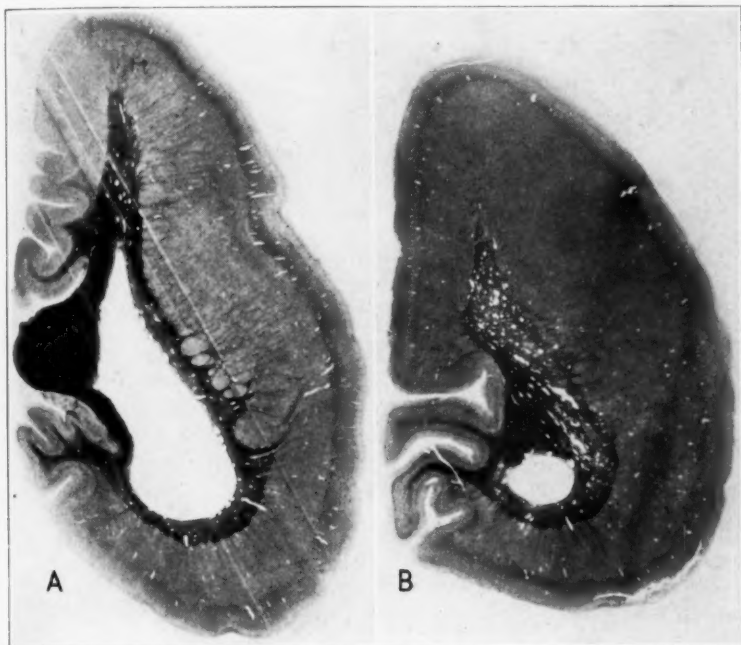


Fig. 5.—*A*, the coronal section through the splenium of the corpus callosum showing no gyri in the occipital lobe except two on the medial posterior surface. Markedly poor myelinization is also shown. Note the gray islands in the white matter as well as the white areas in the ependyma of the lateral ventricles. Dilated ventricle. (Weil stain; photograph.) See figure 12. *B*, the coronal section through the posterior horn of the lateral ventricle, showing the absence of gyration. (Weil stain; photograph.) See figure 12.

areas were still further reduced in size, while the corpus callosum was normally myelinated. The inferior longitudinal fasciculus was fairly well represented. The lateral ventricle was markedly dilated, and there was no choroid plexus. The sulci of the occipital pole were very shallow. The paracentral, cingular and hippocampal gyri were well developed. On the outer aspect of the corona radiata were numerous large and small, circular and oval nonstaining areas surrounded by darkly staining, thin fibers (blue). There were many vacuoles in the corona

radiata and in the gray substance under the ependyma, and a few oval and round nonstaining areas on the outer aspect of the inferior longitudinal fasciculus of the temporal lobe.

A coronal section (fig. 5 *B*) through the posterior horn of the lateral ventricle showed absence of gyri in the occipital lobe. The cuneus, the calcarine fissure and the lingual lobule were well developed. The narrow myelinated area of white matter surrounding the inferior horn of the lateral ventricle was interspersed with, and surrounded by, small unmyelinated islands. The optic radiations stood out, well myelinated.

Pons Medulla Oblongata and Cerebellum: Sections through these structures revealed normal myelinization.

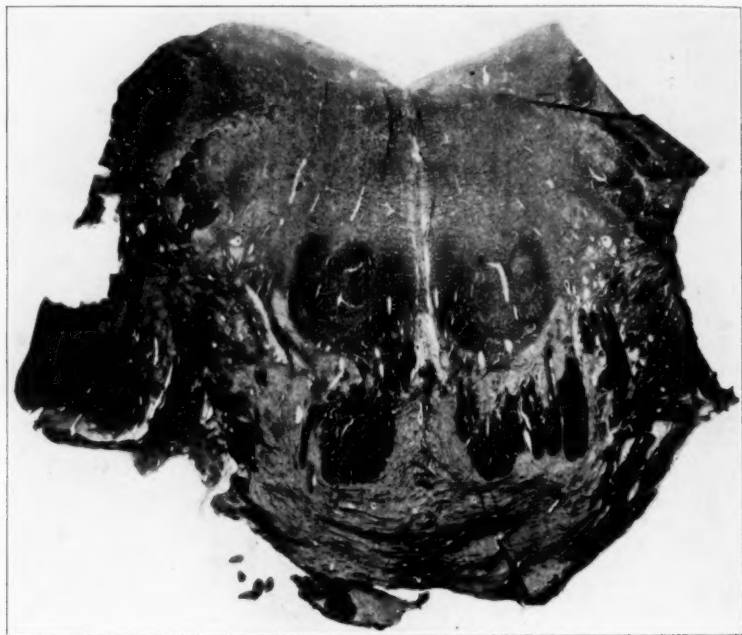


Fig. 6.—Showing the pons to be smaller than normal. No defects are revealed. (Weil stain; photograph.)

Spinal Cord: Horizontal and vertical sections through different segments of the spinal cord showed no abnormalities of myelinization.

Unmyelinated Areas: The homogeneous unmyelinated areas in the coronal sections, already described, showed the following histologic structure: Cresyl violet staining revealed many round glia nuclei and an occasional rod-shaped nucleus; van Gieson preparations showed many glia nuclei, with a dearth of blood vessels; silver preparations (Davenport) revealed many glia nuclei and a decreased number of axons, which appeared to be interrupted; Cajal gold sublimate staining revealed many macroglia (normal).

(*b*) Heterotopia of the Gray Matter: Weil and Kulschitzky-Pal myelin sheath stains revealed an unusual picture. The areas seen macroscopically as brownish red between the cortical gray and white matter were made up of circular or oval



Fig. 7.—The fifth thoracic segment of the cord, showing normal conditions. (Weil stain; photograph.)

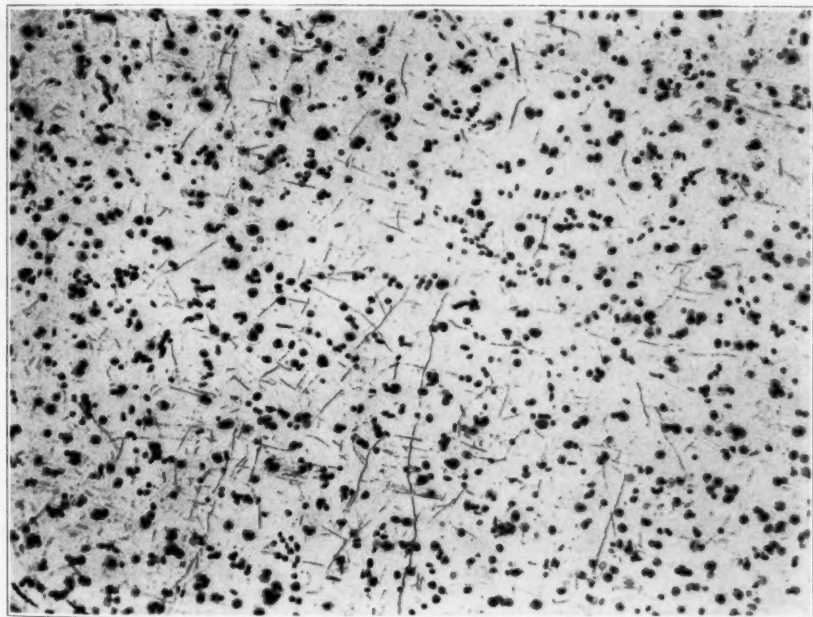


Fig. 8.—An area of white matter from the occipital lobe where no myelinization was seen, showing many round glial nuclei and interrupted axons. (Cajal nerve stain;  $\times 250$ .)

nonstaining zones surrounded by blue-staining fibers extending from the cortex into the white matter. This picture was seen throughout the entire brain between the gray cortex and the white matter.

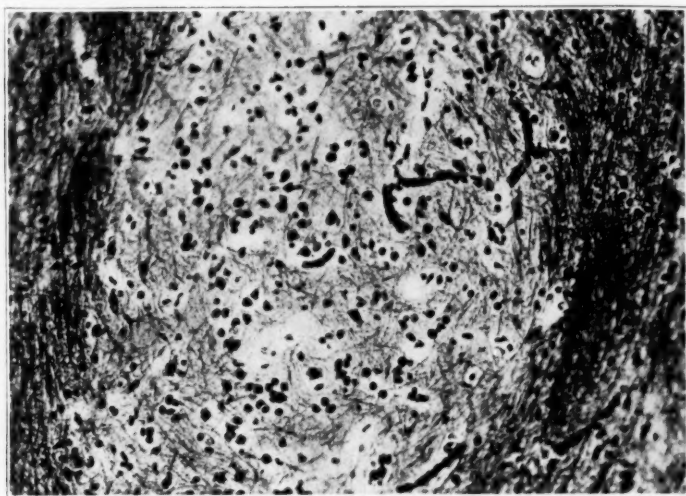


Fig. 9.—Gray island in the white matter (heterotopia) revealing a normal structure of the gray matter. (Cajal nerve stain;  $\times 375$ .)

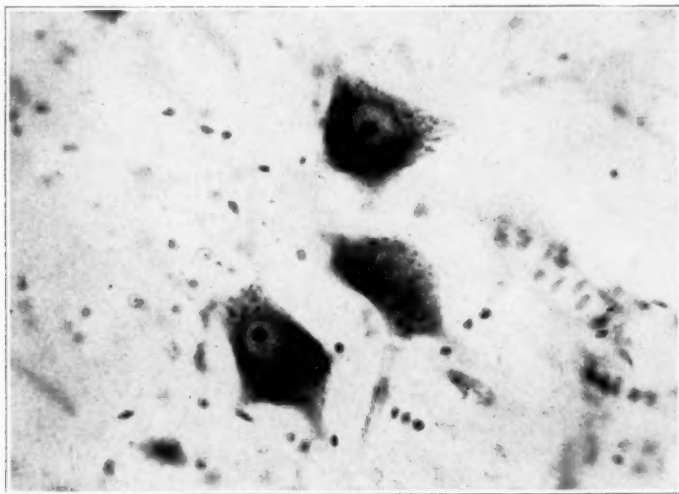


Fig. 10.—Normal ganglion cells found in heterotopic areas. (Cresyl violet;  $\times 650$ .)

The oval, circular and irregularly shaped nonstaining areas already mentioned were collections of ganglion cells, neuroglia cells and capillaries. Nuclear stains of these areas revealed pyramidal cells such as are usually present in the third and fourth layers of the normal cerebral cortex. In these there was a centrally placed

nucleus. Within the nucleus was a nucleolus. There was ample hyaloplasmic substance surrounded by a cell wall, with extension into dendrites and one axon containing neurofibrils. Nissl bodies surrounded the nucleus. Fibrous astrocytes, oligodendroglia and microglia were present in these areas. There was no evidence of change in the nerve cells, such as chromatolysis, or neuroglial abnormality,

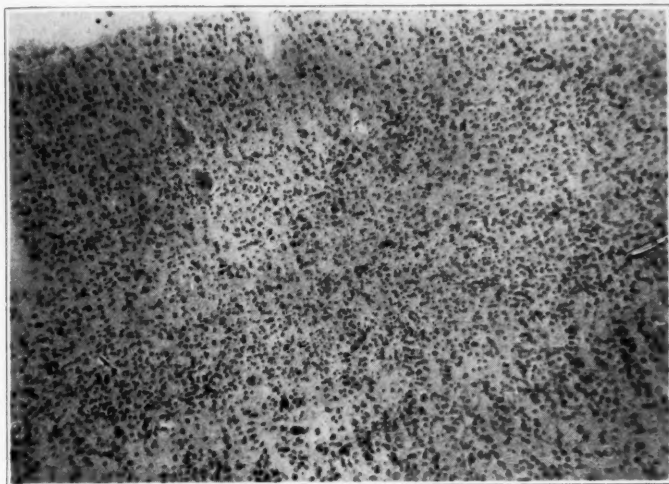


Fig. 11.—Cyto-architectonic structure of the parietal cortex, showing no abnormality. (Cresyl violet;  $\times$  325.)

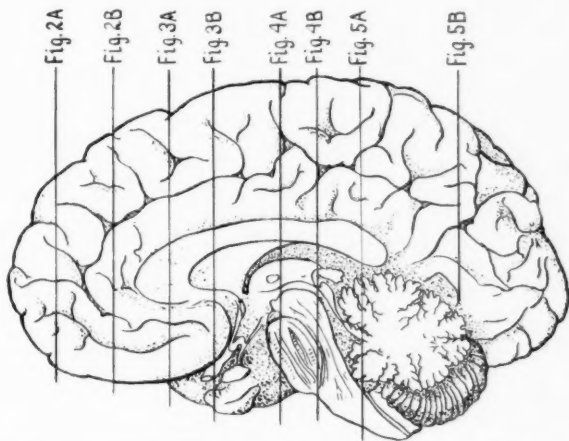


Fig. 12.—The approximate locations of various coronal sections described in the text.

except that the neuroglia cells were slightly larger than normal. No neuronophagia or abnormal satellitosis was seen.

(c) Cyto-Architectonics: The cyto-architectonic structure of the frontal, parietal, temporal and occipital cortices was within normal limits (as compared with von Economo's cyto-architectonic structures). In some sections of the various

cortices the nuclei and cytoplasm did not take so deep a stain as under normal circumstances. Some of the ganglion cells in the large pyramidal cell layer were smaller than normal.

The ependymal cells lining the fourth ventricle and the central canal were of the long columnar type, with one process (embryonic).

*Summary.*—The changes observed may be classified as: microcephaly; undeveloped myelinization, chiefly in the white matter of the occipital and parietal lobes; deposition of islands of gray substance in the white matter of the brain (heterotopia), and cerebral agyria, pachygyria and microgyria.

#### COMMENT

The clinical histories of the three members of a family that we presented as showing familial spastic paralysis are in agreement with those reported in the literature.

The histopathologic changes in familial spastic paralysis were first described by Strümpell<sup>44</sup> in 1886, who mentioned: pure sclerosis of pyramidal tracts and slight degeneration of the tracts of Goll, Flechsig and Gowers; in another case, typical degeneration of the pyramidal tracts, especially in the thoracic and lumbar regions, and a slight degeneration in Goll's tracts, which disappeared in the middle thoracic region. The ganglion cells were normal.

In 1893, Newmark<sup>45</sup> reported two cases in which there were changes in the lateral pyramidal tracts, with involvement of the posterior columns in the cervical region. In one case Betz cells were lacking.

Eichorst<sup>46</sup> reported two cases in which the disease affected mother and son. The former showed numerous sclerotic foci extending from the external border of the white matter of the spinal cord 0.5 mm. inward, involving the anterior and lateral tracts. There was a small cavity in the lower thoracic region in the anterior part of the posterior column extending into the posterior longitudinal fissure and into the central canal. Diffuse sclerosis of the brain was present. In the son, Eichorst found sclerotic changes in the cervical region in the anterior third of the posterior columns and, in the thoracic and upper lumbar regions, in the lateral tracts and anterior tracts. There were nests of atrophic nerve fibers in the anterior and posterior roots along the entire extent of the spinal cord. There were no changes in the brain.

Peskin's<sup>47</sup> case revealed retarded development of the entire fiber system of the spinal cord, including complete absence of the cerebellar and lateral pyramidal tracts and almost complete disappearance of Clarke's column.

Bischoff,<sup>48</sup> in 1902, reported a dearth of fibers in the lateral pyramidal tracts of the spinal cord, increasing toward the dorsal portion; loss of fibers in the

44. Strümpell, A.: Ueber die hereditäre spastische Spinalparalyse, Deutsche Ztschr. f. Nervenhe. **4**:173, 1893.

45. Newmark, Leo: A Contribution to the Study of the Family Form of Spastic Paraplegia, Am. J. M. Sc. **55**:432, 1893.

46. Eichorst, Herman: Ueber infantile und hereditäre Multiplesklerose, Virchow's Arch. f. path. Anat. **46**:173, 1896.

47. Peskin, Aron: Ueber eine eigenthümliche Form familiärer Erkrankung des Centralnervensystems, Berlin, M. Günther, 1900.

48. Bischoff, E.: Pathologisch-anatomischer Befund bei familiärer infantiler spastischer Spinalparalyse, Jahrb. f. Psychiat. **22**:109, 1902.

median portion of Goll's column, and attenuation of fibers of the pyramidal tracts in the medulla oblongata, with increase of glial tissue. The brain was normal.

Baumlin's<sup>49</sup> case showed leptomeningitis in the dorsal and lumbar regions of the spinal cord. In the lower dorsal region there was a slight paleness of the fibers in the outer portion of the marginal zone of the lateral tracts. The cervical region showed a similar condition. The brain was normal.

Bourneville and Cruzon<sup>50</sup> described atrophy of the cerebellum and of the pons and diminution of the fibers of the pyramidal tracts.

Pellizzi,<sup>51</sup> in 1906, mentioned: degeneration of the ganglion cells of the retina; pronounced peripheral chromatolysis, especially in the polymorphous cells; accumulations of yellow pigment in the pyramidal cells; almost complete loss of the fibers of the cortex in the frontal and parietotemporal lobes; sclerosis of the pyramidal tracts, especially in the internal capsule and medulla oblongata, as well as in the crossed and uncrossed pyramidal tracts; sclerosis of Flechsig's and Gowers' tracts and of Lissauer's zones, and slight sclerosis of Goll's tract; marked peripheral chromatolysis of the cells of the anterior horns, especially in the lumbar cord, and a notable reduction and atrophy of the fibers in the corresponding anterior roots; peripheral chromatolysis in the intervertebral lumbosacral ganglia, associated with disappearance of the myelin sheath in some fibers of the related posterior roots.

Brissaud<sup>52</sup> described two cases in brothers showing sclerosis of the pyramidal tracts and of Gowers' tracts, with an almost imperceptible change in Goll's column.

Kollarits<sup>53</sup> described the pathologic changes in the cases previously reported by Jendrassik. He found that the spinal cord was flat, with deep septums. The gray matter was small; the lateral pyramidal columns were bilaterally degenerated, extending to the cervical region, and Goll's column showed only a little change, which was more marked in the center of the dorsal portion. The gastrocnemius muscle showed partial fatty degeneration, with the muscle fibers reduced in width; some normal nerve fibers were present among the diseased ones.

Merzbacher's<sup>54</sup> case showed absence of the medullary sheaths of the white matter of the hemispheres, pons and cerebellum. Only here and there were medullary fibers intact, and then only for a short distance. The fibers of the internal capsule were less affected. There was marked cerebral atrophy due to loss of axis cylinders and of medullary sheaths. Merzbacher believed that the disease was primarily an extracortical manifestation. He suggested the name of "aplasia axialis transcorticalis congenita."

Lederer<sup>55</sup> reported an instance of atrophic spinal cord in which there was a defect in cells and fibers with numerous undeveloped ganglion cells.

49. Baumlin, J.: Ueber familiäre Erkrankungen des Nervensystems, Deutsche Ztschr. f. Nervenhe. **20**:313, 1901.

50. Bourneville and Cruzon: Progrès méd. **30**:272, 1901.

51. Pellizzi, G. B.: Paraplegia spasmodica famigliare e demenza precoce, Riv. sper. de freniat. **32**:1, 1906.

52. Brissaud, E.: Ein Fall von hereditärer Familienerkrankung vom Uebergangstypus zwischen spastischer Spinalparalyse und Friedreichscher Krankheit, in Dobrochotow, Deutsche Ztschr. f. Nervenhe. **5**:49, 1913.

53. Kollarits, J.: Beiträge zur Kenntnis der vererbten Nervenkrankheiten, Deutsche Ztschr. f. Nervenhe. **30**:293, 1906.

54. Merzbacher, L.: Weitere Mitteilungen über eine eigenartige hereditäre familiäre Erkrankung des Zentralnervensystems, Med. Klin. **55**:1952, 1908.

55. Lederer, Richard: Familiäre spastische Paraplegie bei drei Geschwistern, Mitt. d. Gesellsch. f. inn. Med. u. Kinderh. **11**:70, 1912.

The pathologic findings in one of the members of the family reported here are not in accord with those in any of the cases in the literature in which the pathologic condition was studied. Instead of abnormalities in the pyramidal and extrapyramidal tracts, posterior columns or cerebellar pathways, we found definite evidence of poor development of myelin, chiefly in the white matter of the occipital and parietal lobes, with concomitant decrease of the axis cylinders, heterotopia of the gray matter in the white substance of the brain and convolutional abnormality.

Failure of myelinization of certain parts of the brain was one of the outstanding changes. The structures which were normally myelinated in the brain were the corona radiata, the corpus callosum, the internal and external capsules, the fornix and the cerebral peduncles. In the frontal lobes all the association fibers of the corona radiata stained fairly well. In the parietal lobe the "U" fibers failed to take the myelin sheath stain in the region where they are normally situated. In the middle of the temporal lobe the association fibers of the inferior longitudinal fasciculus stained only fairly well, while in the temporal lobe at the beginning of the cornu ammonis the collateral or association fibers failed to take the stain. In the occipital lobes the association fibers failed to take the myelin sheath stain, and the corona radiata contained many vacuolated areas.

It is to be noted that where the association or collateral fibers were not stained there was pachygyria. In the parietal and occipital lobes, where there was no myelinization of the collateral fibers, there was agyria. One might say, on the one hand, that the cortical structures which were concerned with vision and hearing were well developed and, on the other hand, the structures regulating motion and acting as cortical receptors for sensation were not developed. It may be added that all the extrapyramidal structures, as well as the brain stem and the spinal cord, showed a normal histologic make-up.

#### SUMMARY

A detailed survey of the literature on familial spastic paralysis is given. The clinical histories of three members of one family who suffered from the condition are recorded. The histopathologic condition in the oldest member of the group is described in detail.

In this case there were, clinically, spastic paralysis and idiocy, and, pathologically, microcephaly with pachygyria and agyria, absence of association fibers of the parietal and occipital regions of the brain, and heterotopia of the gray substance in the white matter of the cerebrum.

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# REFLEX CHANGES AFTER INJURY TO THE PYRAMIDAL TRACT IN THE MACAQUE, GIBBON AND CHIMPANZEE

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NEW YORK

Since Babinski's discovery<sup>1</sup> of the *signe des orteils*, in 1896, an extensive literature has grown up concerning the pathologic reflexes of the lower extremities in man. Experimental studies, however, have been few, and because of this Fulton and Keller<sup>1</sup> recently undertook to investigate the Babinski reflex in a series of infrahuman primates. Plantar reflexes and motor performance were studied in monkeys, baboons, gibbons and chimpanzees—types which represent ascending stages in the evolutionary scale. They observed, after destruction of the motor area, that a permanent Babinski response could be detected only in the chimpanzee, the highest of the forms examined. Incidentally they found it possible to estimate the degree of cortical dominance in a given form by three criteria: (1) the rate of recovery of voluntary power following ablation of the motor area controlling a limb; (2) the extent of depression of the spinal reflexes produced by such a lesion, and (3) the occurrence and persistence of pathologic reflexes, such as the sign of Babinski. At Dr. Fulton's suggestion it was decided to supplement these observations on the Babinski response by studying in the same primate types the reflexes commonly recognized as "Babinski variants."

## NORMAL RESPONSES

Many writers, as Collier,<sup>2</sup> Friedman,<sup>3</sup> Rabiner and Keschner<sup>4</sup> and Rudolf,<sup>5</sup> in considering the cause of the Babinski phenomenon, have begun with the premise that an extensor reaction of the toes in response to plantar stimulation is normal in monkeys and anthropoid apes, and

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From the Laboratory of Physiology, Yale University School of Medicine.

1. Fulton, J. F., and Keller, A. D.: The Sign of Babinski: A Study of the Evolution of Cortical Dominance in Primates, Springfield, Ill., Charles C. Thomas, Publisher, 1932.

2. Collier, J.: An Investigation on the Plantar Reflex, *Brain* **22**:71, 1899.

3. Friedman, E. D.: On a Possible Significance of the Babinski and Other Pathologic Reflexes, *J. Nerv. & Ment. Dis.* **51**:146, 1920.

4. Rabiner, A., and Keschner, M.: Theory of Mechanism for Babinski Toe Phenomenon, *Arch. Neurol. & Psychiat.* **16**:313 (Sept.) 1926.

5. Rudolf, G. de M.: Phylogenetic Significance of the Plantar Response in Man, *J. Neurol. & Psychopath.* **2**:337, 1922.

that therefore the human extensor response is atavistic. That this is not the case has been adequately shown by Fulton and Keller,<sup>1</sup> who observed that the plantar response of all normal primates, when present, is flexor. The present study of the responses of the toes of these animals to stimulation after the methods of Chaddock, Oppenheim, Schaeffer and Gordon has confirmed this general conclusion.

This error that has crept into the literature makes it necessary to submit a description of the normal reactions to the various maneuvers. These reactions will be described briefly for each of the three primate forms examined. The responses after interruption of innervation of the pyramidal tract to one and to both lower limbs will then be discussed briefly in separate protocols.

Following is a résumé of observations made on nineteen normal macaques (*Pithecus* [*Macacus*] *rhesus*), two gibbons (*Hylobates agilis* and *Hylobates leukogenys*) and six chimpanzees (*Pan Chimpanse*), which were under observation for five months. The full details of the procedures and the varieties of responses will not be given.

*Chaddock.*<sup>6</sup>—This method of stimulation elicited no reflex in the macaque or gibbon. In chimpanzees which had been trained to cooperate the response was one of flexion.

*Schaeffer and Gordon.*—Schaeffer's method<sup>7</sup> invariably resulted in flexion of all the digits in all three species. In the macaque and chimpanzee the method of Gordon<sup>8</sup> resulted in a slight extension of the lateral digits; in the gibbon it produced only weak flexion. If pressure was exerted over the upper third of the leg in the macaque or chimpanzee there was marked extension of all the lateral toes; in the gibbon there was no movement. Participation of the hallux was not regular. The higher the stimulation was applied, therefore, the more likely was one to obtain a normal response of extension. That these responses were purely mechanical was indicated by their failure to change after high section of the sciatic nerve or even one hour after death.

*Oppenheim.*—This procedure<sup>9</sup> resulted in flexion of the toes in all three types of animals. If, during the maneuver, pressure on the leg was also transmitted to the extensors, extension of the lateral toes

6. Chaddock, C. G.: Preliminary Communication Concerning a New Diagnostic Nervous Sign, *Interstate M. J.* **18**:742, 1911; The External Malleolar Sign, *ibid.* **18**:1026, 1911.

7. Schaeffer, M.: Ueber einen antagonistischen Reflex, *Neurol. Centralbl.* **18**:1016, 1899.

8. Gordon, A.: A New Reflex: Paradoxical Flexor Reflex; Its Diagnostic Value, *Am. Med.* **8**:971, 1904.

9. Oppenheim, H.: Zur Pathologie der Hautreflexe an den unteren Extremitäten, *Monatschr. f. Psychiat. u. Neurol.* **12**:421 and 518, 1902.

appeared in the macaque and chimpanzee. Pressure over the lowermost tip of the tibia and the ankle elicited extension and abduction of the hallux. It is apparent that it is easy to obtain mechanical extensor phenomena normally in these animals. As in the human being, these procedures may also evoke extensor movements of defense.<sup>10</sup>

*Rossolimo*<sup>11</sup> and *Mendel-Bechterew*.<sup>12</sup>—A varied response was obtained in eleven of nineteen macaques. In three of seven mature specimens reflex flexion was regularly obtained. The hallux and the region immediately near it seemed to constitute the focal area of the reflex zone, and the hallux also appeared to be the most common recipient of the reflex discharge. In animals in which the response was most easily elicited a slight flexion of the lateral digits was also obtained occasionally. A positive response was obtained in six of nine macaques between the ages of about 6 months and 1 year. Participation of the lateral toes in these was more common than in the older animals. Three infant macaques, varying in age from 1 to 32 days, invariably gave a response of all the toes. Percussion of the dorsum of the foot or the planta regularly elicited flexion of the hallux. These facts suggest that the magnitude and sensitivity of the Rossolimo test are greater in younger animals, but the material at hand was not adequate to allow a complete study of differences in age.

One gibbon on which no operation had been performed was available for study; it failed to show any flexion to either the Rossolimo or the Mendel-Bechterew method of stimulation.

In only three of six chimpanzees was a slight Rossolimo response obtained. This reflex was not constantly present, and its magnitude waxed and waned during the same examination, irrespective of continued stimulation. In two animals there was at times a dorsiflexion of the toes in response to the Mendel-Bechterew procedure. In the other animals there was no response to this maneuver.

10. (a) Goldflam, S.: Sur la valeur clinique du signe de Gordon, *Rev. neurol.* **1**:592, 1925. (b) Rothfeld, J.: Die Dorsalflexion der grossen Zehe als Reaktion auf schmerzhaft Reize, *München. med. Wchnschr.* **65**:21, 1918. (c) Stähle, E.: Das Auftreten des Oppenheimschen Phänomens beim Fünftagefieber und das Pseudo-Oppenheim Phänomen, *ibid.* **64**:1417, 1917.

11. (a) Rossolimo, G. J.: Der Zehenreflex (ein speziell pathologischer Sehnenreflex), *Neurol. Centralbl.* **27**:452, 1908. (b) Nikiteu: Ueber den Beuge-reflex der Zehen, *ibid.* **28**:434, 1909. (c) Goldflam, S.: Die diagnostische Bedeutung des Rossolimoschen Reflexes bei Erkrankungen des Zentralnervensystems, *Abhandl. a. d. Neurol.* **56**:274, 1930.

12. von Bechterew, W.: Ueber einen besonderen Beugereflex der Zehen, *Neurol. Centralbl.* **23**:609, 1904. Mendel, K.: Ein Reflex am Fussrücken, *ibid.* **23**:197, 1904. Yoshimura, K.: Ueber den Mendelschen Fussrückenreflex, *Wien. klin. Rundschau* **22**:309, 1908.

## EXPERIMENTAL MATERIAL

Details of the methods used may be found in the monograph of Fulton and Keller. No autopsy material is presented, since most of the animals were still alive at the time of writing. The full details concerning the ultimate pathologic findings will appear in future communications from Dr. Fulton's laboratory.

## MONKEYS

The lowest primate examined was the common monkey, *Pithecus* [*Macacus*] *rhesus*. Study of the Babinski variants in this form is of considerable interest, since Fulton and Keller<sup>1</sup> have found that the Babinski response itself is absent on the affected side even after destruction of an entire cerebral hemisphere. That the Babinski variants tend to follow the Babinski sign is evident from the two following experiments.

**EXPERIMENT 1.**—A mature male monkey (*Pithecus rhesus*) weighing 9,000 Gm. gave no response to the Rossolimo and Mendel-Bechterew procedures before operation. Simultaneous bilateral destruction of the representations of the lower extremities in the motor cortex was done. There was marked paresis, and the return of motor power was slow. Responses to the Babinski, Chaddock, Oppenheim, Gordon and Schaeffer procedures were negative; a positive response was obtained to the Rossolimo and Mendel-Bechterew tests.

**Operation (April 4, 1932).**—The cortical motor areas for both feet were removed simultaneously after identification by means of monopolar faradic stimulation.

**Postoperative Course.**—During the first two weeks there were signs of extensive cerebral damage owing possibly to clot or edema. During this period the animal was unable to assume the horizontal posture, and Magnus-deKleijn reflexes could be elicited. Power in the limbs returned slowly, but after three months the animal was able to run about and leap great distances.

**Reflexes:** The Babinski, Chaddock, Oppenheim, Gordon and Schaeffer procedures elicited the same responses at all periods following the operation as they had before. However, from the second day after the operation the Rossolimo and Mendel-Bechterew procedures elicited responses of the hallux and rarely of the other toes.

**EXPERIMENT 2.**—The representation of the right lower extremity was extirpated from the motor cortex of a mature male monkey (*Pithecus rhesus*) weighing 6,100 Gm. Focal seizures occurred, and the bone flap was reelevated three days later. There was no change in response to the Babinski, Chaddock, Oppenheim, Gordon and Schaeffer types of stimulation, but there were some differences in response to the Rossolimo and Mendel-Bechterew tests.

Active flexion of the hallux could be obtained with the methods of Rossolimo and Mendel-Bechterew.

**Operation (May 9, 1932).**—A bone flap was turned down on the left side under sodium amytal anesthesia. Moderate bleeding from the superior longitudinal sinus was easily controlled. When the dura was opened a collection of freshly clotted blood was found over the arachnoid, and on its removal a pale cortex was uncovered. The foot area was identified and excised. The rest of the procedure was uneventful.

**Postoperative Course.**—The initial neurologic picture revealed sensory disorders on the right, homonymous hemianopia and weakness of both limbs. Because of

the appearance of jacksonian seizures in the face and arm on the right side the flap was reelevated three days later to determine whether there had been post-operative bleeding. The operative site was, however, clean. After several days the complicating features disappeared, and the subsequent course was uneventful.

**Reflexes:** The responses of both lower limbs to the Babinski, Chaddock, Oppenheim, Gordon and Schaeffer types of stimulation proved to be unaffected by the operation. The Rossolimo and Mendel-Bechterew procedures, however, elicited a slightly more active reflex. The increase in magnitude of response appeared bilaterally a day after operation; it was slightly greater on the right.

**Summary of Experiments 1 and 2.**—In the first animal the removal of the foot area was bilateral, and in the second animal it was unilateral. In neither animal were the responses to the Babinski, Chaddock, Oppenheim, Gordon and Schaeffer types of stimulation altered. In animal 1 the Rossolimo and Mendel-Bechterew reflexes appeared only after operation, and in animal 2 the responses, which were originally present, increased bilaterally, but the increase was slightly greater on the paretic side.

#### THE GIBBON

The gibbon assumes special interest in the problem in hand because it is the only primate other than man which employs an erect biped mode of progression. Its hallux is long and is laterally placed, but, like the rest of the foot, it is essentially plantigrade.

**EXPERIMENT 3.**—*In gibbon 1 (Hylobates agilis), an immature male weighing 2,000 Gm., the plantar responses were flexor. Ablation of the representation of the right lower extremity in the motor cortex resulted in negative reactions to the Schaeffer, Gordon and Oppenheim procedures bilaterally and in flexion on the paretic side following the Rossolimo and Mendel-Bechterew tests; the Babinski sign was present. Ablation of the representation of the left lower limb caused a marked motor deficit. There was a typical Babinski sign bilaterally; the Schaeffer and Gordon responses were flexor in type; the Oppenheim reflex was negative, and the Rossolimo and Mendel-Bechterew signs increased and were equal on the two sides.*

About a month before this study was begun (Jan. 12, 1932) the left hemisphere of gibbon 1 was exposed, the motor cortex mapped by faradic stimulation and the cortical representation of the contralateral lower limb ablated. This procedure and its results were reported in detail by Fulton and Keller<sup>1</sup> and by Fulton and Kennard.<sup>13</sup>

**Reflexes Before Second Operation.**—During this period no pathologic responses were obtained on the paretic side to the Chaddock, Oppenheim, Schaeffer and Gordon types of stimulation. Sometimes extension of the toes occurred as a reaction to pain. The Babinski response, which was completely extensor during the first nine days, changed to one of flexion of the hallux and extension of the lateral toes. The Rossolimo and Mendel-Bechterew procedures, however, regularly evoked flexion whenever the animal could be made to relax. Only rarely could one obtain a suggestion of response from the nonparetic limb.

**Operation (March 24).**—Under sodium amytal anesthesia the representation of the left leg in the right motor cortex was extirpated.

**Reflexes After Second Operation.**—Immediately after the second operation a typical Babinski response associated with withdrawal could be obtained on both sides. For several hours this was more marked on the right side, i. e., ipsilateral to the lesion; thereafter the greater response was elicited from the left extremity.

With return of power the form and magnitude of this response changed gradually (earlier on the right than on the left), so that strong plantar stimulation eventually elicited flexion of the hallux, whereas delicate stimulation caused extension of the hallux.

For the first two days strong stimulation of the Chaddock type applied on either side gave a response of extension and reflex withdrawal on both sides; thereafter voluntary movements appeared regularly on the right and there were no reflex responses on the left.

Only for the first day did the Schaeffer maneuver evoke reflex withdrawal and extension of the toes when the tendo achillis was released. The Gordon and Oppenheim signs were negative.

The Rossolimo and Mendel-Bechterew reflexes showed no changes until a few days after the second operation, after which they could be regularly elicited on both sides, and their magnitude increased from one and one-half to two times. Occasionally a response to Mendel-Bechterew stimulation was elicited even by percussion over the lower third of the tibia on either side. If the reflexes were absent at the beginning of the examination, repeated stimulation evoked them.

*EXPERIMENT 4.*—In gibbon 2 (*Hylobates leucogenys*), an immature female weighing 2,330 Gm., the plantar reflexes were weakly flexor; the Rossolimo and Mendel-Bechterew reflexes were negative. Ablation of the representation of the areas of the right leg in the motor cortex resulted in the immediate appearance of the Babinski and Chaddock reflexes, with reflex withdrawal of the limb. Later the Rossolimo reflex was positive, and the Gordon, Schaeffer and Oppenheim reflexes were negative.

As this animal became seriously ill with diarrhea it was decided to operate on it and kill it soon enough thereafter to obtain Marchi degenerations.

*Operation (April 20, 1932).*—Under sodium amytal anesthesia the left motor cortex was mapped by faradic stimulation and the entire representation of the lower extremity was removed.

*Reflexes.*—The Babinski and Chaddock responses, associated with complete withdrawal of the lower limb, were present on the right at the end of the operation, but five hours later they could not be elicited. The Rossolimo and Mendel-Bechterew responses were absent. On the following day the Babinski response, though still present, was difficult to obtain. The Rossolimo response, however, had become positive, and the Mendel-Bechterew procedure evoked flexion of the hallux only. On subsequent days, until the animal was killed (May 4), strong plantar stimulation would at times produce fleeting, weak extension of the four lateral toes on the right. The Gordon, Schaeffer and Oppenheim procedures gave negative results. The Rossolimo sign, however, could be obtained regularly. Frequently the Mendel-Bechterew sign was also positive, although the extent of movement was variable and of less magnitude.

*Summary of Experiments 3 and 4.*—The responses, the character of which changed definitely after operation in the two animals, were those obtained with the Babinski, Chaddock, Rossolimo and Mendel-Bechterew types of stimulation.

The Schaeffer maneuver invariably elicited flexion of the toes. Only for a few hours after bilateral ablation on the first animal did such stimulation elicit reflex withdrawal and a complete Babinski phenomenon; however, this appeared only after the tendon was released, for while pressure was exerted the toes persisted in flexion.

The Gordon maneuver elicited either limited flexion of the digits or no response at all. A positive response to the Oppenheim procedure was obtained

only when some voluntary power was exercised and when pain was inflicted during the procedure. This was very likely a pseudo-Oppenheim<sup>10b,c</sup> phenomenon.

The Chaddock sign was obtained in gibbon 2 following unilateral destruction of the pyramidal fibers to the lower limb. Its relation to the Babinski phenomenon could not be adequately followed in this animal because both responses disappeared almost completely on the day after the operation, owing to shock. In the first animal the results of bilateral extirpation indicated that the skin on the dorso-lateral surface of the foot was relatively insensitive and required strong stimulation to elicit a pathologic response. Furthermore, within two days the sensitivity of this zone to stimulation diminished so much that only the most intense stimuli caused a reaction, which was then only one to pain. The area of response to lateral plantar stimulation, however, had enlarged and had become practically constant.

The Rossolimo and Mendel-Bechterew phenomena appeared on the contralateral side following unilateral lesions in both animals. The Rossolimo sign was the more marked. It is possible that the delicate and inconstant responses, which were observed in the nonparetic limb of the first animal after unilateral ablation of the foot area, were due to destruction of the few physiologically active<sup>1</sup> ipsilateral pyramidal fibers. After bilateral ablation the extent and sensitivity of both reflexes in each foot increased to almost twice the amplitude of the reflexes formerly seen in the right foot.

#### THE CHIMPANZEE

Of the three primate forms under investigation the chimpanzee is nearest to man in the evolutionary scale and is therefore the most significant subject for experimental studies designed to elucidate problems of clinical neurology.

*EXPERIMENT 5.*—In an immature male chimpanzee (*Pan Chimpanse*) weighing 12,000 Gm. the representation of the area of the left foot in the motor cortex was extirpated. A contralateral Babinski response was obtained after twenty-four hours. Studies made after twenty-five days showed positive Chaddock, Rossolimo and Mendel-Bechterew reflexes on the right. Removal of the cortical representation of the area of the right foot after an interval of six weeks resulted in a marked motor deficit, with permanent and increased bilateral Babinski, Chaddock, Rossolimo and Mendel-Bechterew signs. The Oppenheim sign was doubtful. The Schaeffer and Gordon signs were negative.

This animal was intelligent, well trained and cooperative to a remarkable degree. The representation of the leg in the left motor cortex had been ablated twenty-five days before the present study was begun. The Babinski response was positive twenty-four hours after the operation<sup>1</sup> and remained so.

*Reflexes Before Second Operation.*—The focal region for the Chaddock reflex lay along the extreme dorsolateral area of the foot and fused at its lateral margin with the focal area for the Babinski sign. The response was the same as the typical Babinski sign except that the latter showed less clonic after-discharge.

On the paretic side the Rossolimo sign was constant and increased regularly to a maximum response on continued stimulation. Its focal area of responsiveness to percussion covered the plantar surfaces of the three middle metatarsal bones. Stimulation over the plantar surfaces of the first and fifth metatarsal bones yielded flexion of the corresponding toes only, but frequently there was a typical response. On the nonparetic side a weak, inconstant movement, similar to that in normal animals, was occasionally seen. The differences between the two sides were marked.

On the sound side the Mendel-Bechterew type of stimulation often caused extension of the first two toes at the metatarsophalangeal joints; in the paretic limb plantar flexion of the toes occurred. Stimulation over the first and fifth metatarsal bones might result, as in the Rossolimo test, in flexion of the corresponding toes, but percussion over the three middle metatarsal bones and the tarsal bones adjoining them usually resulted in a complete response which resembled the Rossolimo sign, though it was neither so active nor so regularly obtained.

The Oppenheim reflex differed little from the normal response. Only rarely did the hallux participate and then only in response to pressure applied low on the tibia near the ankle.

The Schaeffer and Gordon responses were never different from those seen in the normal animal.

*Second Operation (March 4).*—Under sodium amytal anesthesia a generous extirpation of the representation of the second lower extremity in the right motor cortex was made.

*Reflexes After Second Operation.*—Immediately following the second operation all reflexes disappeared on both sides. On the right the Chaddock sign reappeared almost simultaneously with the Babinski on the morning of the first day after the operation and was more vigorous than the Babinski response. The Rossolimo and Mendel-Bechterew signs were obtained shortly thereafter. In the left limb all these signs appeared between the second and the third day following the operation. These reflexes increased in magnitude and sensitivity until the fifteenth day, when the responses on the two sides were approximately equal. This steady state was attained more quickly on the right side, where the effects of shock due to the destruction of uncrossed pyramidal fibers were less.<sup>1</sup>

Following is a brief summary of the results after the reflexes had become fully developed and equal on the two sides.

The reflex zone of the Chaddock sign extended to involve the whole of the dorsum of the foot. The focal area of the Babinski sign widened, and the reflex manifested itself in its most complete form (Fulton and Keller<sup>1</sup>). The Chaddock response was of similar magnitude. Although there was less tendency to reflex withdrawal of the whole limb as power returned, vestiges of the response, especially dorsiflexion of the foot, remained. The only difference between the Chaddock and Babinski reflexes was that the Babinski reflex was followed by a less clonic after-discharge.

When both reflexes had become well established, contralateral reflex phenomena were obtained regularly by vigorous and prolonged stimulation of the planta or the dorsolateral surface of the foot. The crossed response generally appeared as extension at the knee several seconds after the homolateral flexor reflex. If stimulation ceased at this point no further response ensued, but if it continued extension of the leg became complete and was followed successively by abduction of the thigh, plantar flexion at the ankle and extension and abduction of all the toes. As the movement developed it picked up speed, and on completion the extensor position of the contralateral limb was maintained tonically for several seconds. On repeated stimulation the latent period and the intensity of stimulation necessary to evoke this phenomenon lessened. Sometimes, after crossed extension had been maintained for a while, it gave way to an aborted flexor reflex. Less frequently, crossed extension at the knee was interrupted in its earlier stages by the appearance of flexor phenomena originating at the toes and ankle. On continued stimulation, however, extension of the contralateral limb reasserted itself. Rarely, crossed extension was not evoked; but instead there appeared a

flexor reflex with a fully developed Babinski sign, after a latent period somewhat longer than that of the crossed extensor response.

The magnitude of the Rossolimo response was doubled, and that of the Mendel-Bechterew response was approximately trebled. The reflex zones of both widened so extensively that responses to percussion could be obtained from the anterior, medial and posterior surfaces of the entire thigh and even to percussion over the muscular mass in the region of the anterior superior spine of the ilium. In time this zone shrank so that percussion over the lateral surface of the leg and the anterior surface of the thigh gave less constant responses. Stimulation along the posterior aspect of the thigh generally evoked a slightly stronger response than percussion over the anterior surface.

The Schaeffer and Gordon responses did not change. Extension of the hallux to the Oppenheim procedure occurred rarely on stimulation of the lower third of the tibia; it was variable and was obtained with difficulty.

*Summary of Experiment 5.*—A response resembling the typical Babinski sign in all essentials was obtained from the Chaddock zone after ablation of the opposite foot area in the motor cortex of the chimpanzee. Its magnitude and sensitivity were about equal to those of the Babinski sign; both persisted permanently (i. e., they were still present six months after the second operation). Following removal of the second foot area both responses became enlarged to an equal degree, and crossed extension and flexion reflexes were obtainable from their reflex zones on appropriate stimulation, if sufficiently prolonged.

There are many indications that the sign of Chaddock is in reality a part of the Babinski sign, the reflex zone having merely extended over the lateral edge and up the dorsolateral surface of the foot. In support of this theory are the facts that the focal areas of the two signs fuse at the lateral margin of the foot and that an increase in the extent of a lesion of the pyramidal tract, or the effects of facilitation, causes these zones to enlarge in a direction away from this region. The other points of resemblance are too obvious to require repetition.

The Rossolimo and Mendel-Bechterew signs seem to run a similar course. Following unilateral ablation the former was present to a well marked degree in the contralateral limb. It was obtained regularly, and both its magnitude and the area of its reflex zone increased to a maximum point after continued stimulation. The Mendel-Bechterew sign was less constant and was not always as clearly demonstrable; but it changed from a response of extension to one of flexion, and in all other respects it resembled the Rossolimo sign. Following the second operation the magnitude of both signs increased remarkably on both sides, and their respective reflex zones fused and became indistinguishable above the level of the ankle. The Rossolimo procedure elicited flexion of the toes of the widest excursion. The development and increase in the size of the Babinski, Chaddock, Rossolimo and Mendel-Bechterew phenomena were in a certain sense proportionate.

The Schaeffer and Gordon responses never altered significantly. The Oppenheim sign was at best doubtful and was difficult to obtain even after the second operation.

#### GENERAL COMMENT AND SUMMARY

The Chaddock, Oppenheim, Gordon and Schaeffer signs are the generally recognized equivalents of the Babinski sign. None of their positive homologs was recognized in the normal macaque, gibbon and chimpanzee.

The lowest primate examined was the macaque. No change in the responses to these types of stimulation was apparent in this form after unilateral and bilateral ablation of the cortical motor representation of the lower extremities. Their absence in only two animals studied, following such experimental lesions, is not proof that they may not be found in other macaques similarly treated. These observations are, however, clearly significant when one views the similar results obtained by Fulton and Keller<sup>1</sup> with the plantar reflex in macaques and three other species of monkeys following similar ablation.

In the gibbon, which is higher in the evolutionary scale, a positive Chaddock sign was obtainable on the contralateral side following unilateral ablation of the foot area. Its relation to the Babinski sign could not be adequately studied in gibbon 2 because of "shock" phenomena which persisted in this limb until death. The relationship was more apparent in gibbon 1 after the second foot area was removed. In this animal the Chaddock sign disappeared after a few days, although the Babinski sign persisted permanently in a more or less modified form. This indicates how much more sensitive the lateral aspect of the planta is as compared with the inframalleolar zone in this animal.

The only other positive index of destruction of the pyramidal tract in the gibbon was the sign of Schaeffer. This, however, was of little value, nor did it conform to the reflex as originally described, for even after the pyramidal fibers were totally removed following bilateral ablation, pressure on the tendo achillis sufficed to elicit extension of the toes only for a few hours and only after the tendon was released. The Gordon and Oppenheim signs were absent.

In the chimpanzee, which is nearer man than any other existing primate except, possibly, the gorilla, the Babinski and Chaddock signs were almost equally and classically developed following ablation of the contralateral foot area. After removal of all the pyramidal fibers with destruction of the second foot area, the magnitude and sensitivity of both signs increased, and crossed extension and flexion phenomena could be elicited from their receptive zones to an equal degree from either side.

The Oppenheim sign was equivocal following unilateral extirpation and was no more positive after removal of the motor representation from the other side. The Schaeffer and Gordon signs were invariably negative.

That the Rossolimo and Mendel-Bechterew phenomena should be considered in a category separate from the Babinski variants has been indicated by the results of the extensive work of Goldflam. They are essentially tendon, muscle and periosteal reflexes which are elicited by other than nociceptive stimuli, and they evoke a discharge which differs

from the Babinski sign and its variants. Although the responses in the two macaques from which the excitable foot areas were completely removed (from one hemisphere in the one, and from both in the other) were greater after the operation than before, one cannot conclude that these responses are to be classed with the pathologic reflexes instead of with those which, like the knee jerk, become exaggerated after such lesions. The reason for this is the fact that responses of a similar degree and nature have been found in normal animals of the same species. Such an interpretation, however, fails to explain why percussion over the dorsum of the foot should elicit flexion instead of extension of the hallux, but this is a peculiarity of the sign of the reflex which occurs even normally when the reflex is present. It is of interest that these reflexes were fully developed and were found regularly in three healthy macaques during the first month of life. Although this conforms with Goldflam's findings in normal human infants during the first month, after which these reflexes tend to disappear, a comparison between the human infant and the macaque is scarcely possible when one considers the difference in their relative ages and in the relative degree of cortical dominance. For the present these responses cannot be considered in the category of pathologic reflexes in this animal.

In the two gibbons and in the chimpanzee the findings were different. In the former, following unilateral extirpation of one foot area there appeared an unequivocal Rossolimo sign and a somewhat less active Mendel-Bechterew sign. After removal of the second foot area both responses increased in magnitude bilaterally. In the chimpanzee the results were similar but were more striking; moreover, the sign of the normal response of extension to the Mendel-Bechterew procedure changed to one of flexion.

Since the evidence indicates that circumscribed destruction of parts of the precentral gyrus leads to a degeneration which is limited in the brain stem and cord to the corresponding crossed and uncrossed pyramidal fibers, it is not unreasonable to believe that the regular appearance and constancy of the Rossolimo and Mendel-Bechterew phenomena are connected in some way with impairment of function of these pathways, and that within certain limits the magnitude and sensitivity of these reflexes vary directly with the amount of damage to the motor projection systems from the cortex.

It is reasonable to conclude that these reflexes in the gibbon and chimpanzee have a significance which is different from that of the simple knee jerk. Otherwise it would be difficult to understand why dorsiflexion of the toes, which one often sees in the normal chimpanzee following the Mendel-Bechterew procedure, should change in sign following a lesion of the pyramidal tract. Another fact that lends support to this conclusion is the remarkable extension of the receptive zones for

these reflexes following bilateral extirpation of the foot area in this animal.

In his discussion of the manifestations of the Rossolimo reflex in the human being, Goldflam<sup>11c</sup> stated that he doubted the pathologic significance of a response which is not constant during the period of examination and does not increase to a maximum on continued stimulation and reenforcement. In the chimpanzee three of six normal animals had inconstant, weak responses, which were of a definitely reflex nature. Although a distinction between these responses and those which manifest themselves after lesions of the motor foot area may have a clinical value in these animals, the absolute separation of the two on these grounds alone is artificial from a neurophysiologic point of view. It is possible, however, that future work may shed more light on this problem and connect these two types of manifestation more intimately by revealing the different influences that affect the final common pathways involved.

Clinical experience is rich in a demonstration of the fact that the Babinski variants are frequently demonstrable in the absence of either the Rossolimo or the Mendel-Bechterew sign or of both. The converse of this is also true. This dissociation has been studied in large groups of diseases of the central nervous system in man by Goldflam, who came to the conclusion that varying types of dissociation are more or less characteristic of certain pathologic processes at certain stages of their development and often permanently. After correlating these findings with the pathologic picture characteristic of these processes and, frequently, with definitely localized lesions, he concluded that the Rossolimo and Mendel-Bechterew reflexes, which discharge through the same final common pathway, are signs of a release from a pathway other than the pyramidal tract which courses beside the latter in the lateral columns of the cord ("seine absteigende Bahn ist nicht identisch mit der Pyramidenbahn, dürfte aber in der Nachbarschaft derselben, im Seitenstrang, verlaufen. Der Rossolimosche Reflex ist somit nicht das Zeichen einer Py.-Läsion").

My limited experience following unilateral ablation of the foot area of the motor cortex in the gibbon and chimpanzee, which is followed by degeneration of the pyramidal tract, indicates that the Babinski and Rossolimo (and, to a lesser extent, the Mendel-Bechterew) reflexes are equally<sup>13</sup> developed so far as they are comparable; and that after

13. In the second gibbon the Rossolimo sign was more fully developed than the Babinski sign, which was exceedingly difficult to obtain, but here the dissociation may be explained on the ground that the final common pathway of the one was less sensitive to the effects of shock than was that of the other. This is true generally of tendon phenomena, probably because they are evoked by volleys of impulses which reach the spinal cord with virtual simultaneity.

removal of the other foot area, which is associated with additional degeneration of the pyramidal tract bilaterally, all three reflexes increase to a maximum degree on both sides. I am inclined, therefore, to associate the unequivocal appearance of the Rossolimo and Mendel-Bechterew reflexes with a lesion of the pyramidal pathway instead of with another unknown tract that runs near and with it in the lateral column and which has its origin, according to Goldflam, in the same part of the precentral gyrus and the cells of the frontal lobe adjoining it. One may suspect that the facts submitted by Goldflam are capable of interpretations other than those which he has offered. Much additional experimental work with these reflexes is needed, and possibly methods such as have been used in Sherrington's laboratory for the study of the flexor reflex may be required to elucidate the ultimate meaning of the Rossolimo and Mendel-Bechterew phenomena. Why these two are so often dissociated from the Babinski sign in certain diseases of the central nervous system of human beings is still not clear.

#### CONCLUSIONS

1. The Rossolimo and Mendel-Bechterew signs, being tendon reflexes, must be considered in a category separate from the Babinski variants. Nevertheless, their presence in the gibbon and chimpanzee seems to be a trustworthy sign of organic impairment of the pyramidal tracts. Although similar damage to the pyramidal tracts in the macaque increases these reflexes, their presence in the normal macaque does not permit a similar conclusion for this form.

2. The absence of the Babinski variants following removal of the pyramidal control of the lower limbs in the macaque is in keeping with Fulton and Keller's finding that the plantar response fails to change after removal of such control in the macaque.

3. In the gibbon and chimpanzee the only sign other than the Babinski, Rossolimo and Mendel-Bechterew which has an unequivocal value as an index of damage of the pyramidal tract is the Chaddock sign. This seems to be in reality a part of the Babinski sign, if one regards the reflex zone as having merely extended over the lateral edge and up the dorsolateral surface of the foot.

## DISTURBANCES IN VISUOMOTOR GESTALT FUNCTION

IN ORGANIC BRAIN DISEASE ASSOCIATED WITH SENSORY APHASIA

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The study of disturbances in the perceptual motor *Gestalten* involved in copying figures, as these disturbances appear in cases of organic brain disease associated with sensory aphasia, is of importance both to the theory of *Gestalt* psychology and to the understanding of some problems of optic agnosia in relation to sensory aphasia. An approach to the study of *Gestalt* psychology from the genetic, developmental and pathologic side has been made in my studies in mentally defective and schizophrenic persons<sup>1</sup> and in the sidewalk drawings of children.<sup>2</sup> A more extensive study of the development of *Gestalten* in children suggests itself and is now in preparation. This paper is the first in a series of studies of the disturbances of *Gestalten* in organic and toxic brain diseases and will be followed by similar reports on dementia paralytica, traumatic and alcoholic Korsakoff's syndrome and allied conditions.

*Gestalt* psychology of the Berlin school (Wertheimer-Koehler-Koffka) claims that organized units or structuralized configurations are the primary forms of biologic reactions, at least at the psychologic level of animal behavior, and that in the sensory field these organized units or *Gestalten* correspond to configurations of the stimulating external world.

Classical neurology and the association school of psychology, on the contrary, teach that the function of nerve tissue is the reception of sensory stimuli by sensory endings and the propagation of the resulting impulse, presumably unmodified, over the nerve fiber to the motor or other efferent organ. Sherrington<sup>3</sup> emphasized the integrative action

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1. Bender, L.: Principles of Gestalt in Copied Form in Mentally Defective and Schizophrenic Persons, *Arch. Neurol. & Psychiat.* **27**: 661 (March) 1932; Gestalt in Mental Defect, *Proc. Am. A.* Study of Feeble-minded, 1933, to be published.

2. Bender, L.: Gestalt Principles in Sidewalk Drawings and Games of Children, *Pedagog. Sem. & J. Genetic Psychol.* **41**: 192, 1932.

3. Sherrington, C. S.: *The Integrative Action of the Nervous System*, New Haven, Conn., Yale University Press, 1906.

of the nervous system as a function of the reflex arc, with plurireceptive summation and interference through the synapses converging on the final common path. In some way, however, he recognized that the threshold of the sensory ending may form patterns by selection of modes of stimuli, and he recognized patterns of integrated reactions, accounting for purposeful responses. Lashley,<sup>4</sup> more in sympathy with the recent *Gestalt* teachings, attributed to the final common path the capacity to be sensitized to spatial and temporal patterns which arise from excitations in the sensory endings as a characteristic of integrated behavior. Psychologic data, according to the association school of psychology, are said to arise from simple sensory impressions which are secondarily organized, by combination in the various centers or groups of synapses of the central nervous system, into a mosaic to which meaning is added by association to give experience of the world as one knows it. *Gestalt* psychology, however, has brought evidence to show that organized units or configurations or *Gestalten* are the units of psychologic data, and that their perception and integration are the primary function of the nervous system at every level, including the first sensory level. According to Koehler,<sup>5</sup> the sensory field is organized by the relative properties of the stimulation through a process of dynamic self-distribution in the stimulating field into functional wholes which precede their parts. He contended that the "mutual relatedness" of qualities is a primary fact of perception. "All experienced order in space is a true representation of a corresponding order in the underlying dynamical context of physiological processes." Structuralization is thus a psychophysical process, physiologically determined. Koffka<sup>6</sup> also said that the physiologic process is structural. "Structures, then, (*Gestalten*) are very elementary reactions which phenomenally are not composed of constituent elements; their members being what they are by virtue of . . . their place in the whole." Schilder<sup>7</sup> went beyond the Berlin school with their doctrine of the *Gestalt* function fixed and established as a physiologic process at the perceptive level; he claimed that the *Gestalt* which is already present in sensation builds itself up more and more in the nervous system. "There is not only a shape but a shaping."

4. Lashley, K. S.: *Brain Mechanisms and Intelligence*, Chicago, University of Chicago Press, 1929.

5. Koehler, W.: *Gestalt Psychology*, New York, Horace Liveright, Inc., 1929; *Some Tasks of Gestalt Psychology in Psychologies of 1930*, Worcester, Mass., Clark University Press, 1930.

6. Koffka, K.: *Perception: An Introduction to the Gestalt Theory*, Psychol. Bull. **19**:531, 1922.

7. Schilder, Paul: *Medizinische Psychologie für Aerzte und Psychologen*, Berlin, Julius Springer, 1924.

The higher centers of the cerebrum probably serve as centers of more intricate types of organization, with a tendency to localization of function about the specialized sensory fields. So far, organization or structuralization in the cortical sensory fields has been the main subject of interest in the *Gestalt* studied. That lower centers, such as those of the spinal cord and peripheral nerves, also deal with totally integrated material has been shown by Bromberg and Schilder<sup>8</sup> and by Bromberg in tactile sensibility.<sup>9</sup> It has also been shown, by Schilder and Bender,<sup>10</sup> that lesions in the peripheral nerves and spinal cord will cause disturbances in the *Gestalt* function of this field.

The problem of this study is to determine whether organic brain disease which tends to disorganize cerebral functions will reduce the sensory experiences to independent disconnected sensations or to simpler levels of integration of whole figures. The teaching of the *Gestalt* school would lead one to assume that wherever there is any experience or nervous reaction some power of structuralization persists. Gelb and Goldstein<sup>11</sup> reported the case of a patient who, following a cerebral injury, could not recognize the most elementary *Gestalten*, such as a triangle, or straight or curved lines; they believed that the loss of such *Gestalt* perception is the cause of the symptoms of agnosia, especially alexia. Holmes and Horrax<sup>12</sup> reported the case of a patient, with optic agnosia associated with lesions in the bilateral angular gyri, who had difficulties in orientation in space and who could see things as wholes, but could not analyze them into parts or perceive two adjacent objects in their relationship to each other. Riddoch<sup>13</sup> reported the case of a patient with a bullet wound in the right occipital lobe who could not localize objects in space and could not separate them from their background. Something of this problem has been approached in my studies of normal, defective and schizophrenic persons. These showed that the optic field is in a state of flux or movement and that optic perception arises in it from the vortical movement, which becomes progressively organized: first by perseveration of vortical, whirling or circular move-

8. Bromberg, W., and Schilder, Paul: On Tactile Imagination and Tactile After-Effects, *J. Ment. & Nerv. Dis.* **76**:1 and 133, 1932.

9. Bromberg, W.: Tactual Perception in Alcoholism, *Arch. Neurol. & Psychiat.* **28**:37 (July) 1932.

10. Schilder, P., and Bender, L.: Streuung und Reihenverminderung im sensiblen Abbau, *Deutsche Ztschr. f. Nervenhe.* **129**:146, 1933.

11. Gelb, A., and Goldstein, K.: Psychologische Analysen hirnpathologischer Fälle auf Grund von Untersuchungen Hirnverletzter, *Ztschr. f. Psychol. u. Physiol. d. Sinnesorg.* (I. Abt.) **84**:67 and 193, 1920.

12. Holmes, G., and Horrax, G.: Disturbances of Spatial Orientation and Visual Attention, With Loss of Stereoscopic Vision, *Arch. Neurol. & Psychiat.* **1**:385 (April) 1919.

13. Riddoch, H.: Dissociation in Visual Perception, *Brain* **40**:14, 1917

ment; then by accentuation of radiational movement especially in the horizontal plane, by a separation out of segments, and finally by a control of perseveration by inhibition and the gradual building up of parts derived from these elements as they tend to coincide with external stimuli. In defective adults there is a retardation at the different levels of integration of *Gestalten*, while in schizophrenic persons there is a dissociation of the integrative function. Similarly, the spontaneous sidewalk drawings and games of children<sup>2</sup> show the tendency to maturation of integrative functions established at each age level by an equilibrium between the mental symbols determined by the biologic background of the sensory motor fields and the reality of the external world. These findings lead to the conclusion that the principles of *Gestalt* are not fixed and established by the rules of Wertheimer's<sup>14</sup> *gute Gestalt*, e. g., by proximity, continuity, similarity, inclusiveness and natural geometric figures, but depend in part on the biologic characteristics of the sensory fields at the different maturation levels and the integrative integrity of the functioning nervous system. It is the contention of the Berlin school of *Gestalt* that the *Gestalten* are established by organization in the sensory fields; they are not thought to be completely organized in the stimuli and simply projected on the sense organ, but the organization is something that originates as a physiologic characteristic of the nervous system. Undoubtedly organic integration is, in the last analysis, based on the same principles as those of the so-called inorganic world which furnishes the stimuli; the organism is therefore prepared to organize the data coming from the physical world in accordance with reality as though it were repeating the history of its own evolution. Koehler,<sup>5</sup> it is true, conceded that "attitude" by selection and suppression in some way influences the organization in the sensory field. But one must go further than Wertheimer and Koehler and say, with Schilder<sup>15</sup> and Sander,<sup>16</sup> that the personal complexes, the training and the specific situation also help to determine the organization of each *Gestalt*, and that the *Gestalt* function or integration is not completed at the sensory level but is an active and progressive function of all parts of the nervous system, with a possible tendency, as will be shown in the course of this study, to localize in specialized fields in the cerebral cortex. Fundamentally, then, just as a *Gestalt* arises from a state of flux in the sensory field, so it is always in a state of flux; it is never abso-

14. Wertheimer, M.: Studies in the Theory of Gestalt, *Psychol. Forsch.* 4:300, 1923.

15. Schilder, Paul: Brain and Personality, Nervous and Mental Disease Monograph 53, Washington, D. C., Nervous and Mental Disease Publishing Company, 1931; footnote 7.

16. Sander, F.: Structure, Totality of Experience and Gestalt Psychologies of 1930, Worcester, Mass., Clark University Press, 1930.

lutely determined and is constantly subject to modification depending on the nature of the stimuli, the reception in the sensory organ and sensory field, the state of the nervous system in the different levels through which it passes, the totality of the personality, including the emotional complexes, and the situation or context in which the reaction occurs. In children it is clear that the integrative functions undergo processes of maturation.<sup>2</sup> In the present study, I am interested in following related disintegrating processes in the perpetual motor patterns as they appear in persons with organic brain disease and symptoms of sensory aphasia, and in following the reintegrating processes in the *Gestalten* as there is evidence of recovery from the aphasia.

Sensory aphasia due to left cortical injury was first carefully analyzed by Wernicke,<sup>17</sup> who, in discussing the speech functions of the area known by his name, claimed that the "concrete concept" of an object is a fictional or schematic conception of such an object arising as a function of radiating subcortical fibers from various sensory centers which converge into one point, a sensory speech center, and give rise to a definite group of memory images."

"Loss of memory images from a lesion in this center of the fibers radiating to it" is the classic explanation of sensory aphasia. Hughlings Jackson (cited by Head<sup>18</sup>), however, claimed that the speechless person had not lost the memory for words, but was unable to produce words in propositional speech. The difficulty was thus not one of general intelligence, but of certain activities of the mind having to do with the formation of propositions.

Head<sup>19</sup> defined aphasia as a functional disturbance of speech consequent on a unilateral brain lesion. He denied any significance of the distinction between motor and sensory aphasia because, since speech is an integrative function standing higher in the neural hierarchy than motion and sensation, it cannot be analyzed in terms of motion and sensation. Like Jackson, he did not believe speech to be a general intellectual capacity, but defined it as an act of "symbolic formulation and expression." Aphasia is a defect in the special mental activity of symbolic expression such that the greatest difficulty will occur in higher propositional speech or more abstract symbolization; it is not a defect in general intelligence. Agnosia is a perceptual defect on a lower functional level than that of symbolic formulation and expression.

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17. Wernicke, C.: The Complex of Symptoms of Aphasia, in *Deutsche Klinik am Eingange des Zwanigsten Jahrhunderts in akademischen Vorlesungen*, Berlin, Urban & Schwarzenberg, 1903.

18. Head, Henry: Hughlings Jackson on Aphasias and Kindred Disorders of Speech, *Brain* **38**:1, 1915.

19. Head, H.: *Aphasias and Kindred Disorders of Speech*, New York, The Macmillan Company, 1926.

Head tended to emphasize the formulative and expressive side of speech rather than the integrative, and the symbol as a unit of expression rather than as a part of the symbolic significance of the whole. For this reason perhaps, he did not consider speech as a part of the higher integrative function, which is after all general intelligence and which would tend to rise and fall together with speech in lesions of the cerebral centers. He did, however, recognize that in aphasia the symbol is affected so far as it expresses relational processes in constructive thinking. The other problem to be considered in this connection is whether speech is a specific localizable function of certain cortical areas. Head argued against this, claiming that there is no point-to-point correspondence between the normal production of any psychic act and the independent activity of any particular group of cells. Such centers are solely integrating foci. When they are affected, certain adaptive reactions are disturbed. In other words, as the vigilance dies down, various forms of response disappear. Vigilance seems in some way to express the tone of the nervous activity which functions by way of integration and expresses itself in intelligence on the psychic side. Focal brain lesions prevent the normal fulfilment of some specific form of behavior, but nevertheless the reaction that follows any given situation still expresses the response of the organism-as-a-whole under the new conditions, or, one may say, the new-organism-as-a-whole, which is, perhaps, reacting at a lower organized level or like a more primitive organism.

The recognition of speech as an integrative response of the organism as a whole was more fully emphasized by Schilder.<sup>15</sup> He considered speech as a whole psychic interaction based on symbolic thinking; in aphasia the act of thinking as a whole is disturbed, owing to lesions involving different partial functions, but the nucleus of thinking or conceptional images is not destroyed. There is an obstruction in the development of progressive integration of the sensory cognition, leaving the rest of the brain to function in a more primitive way; nothing is subtracted, but more primitive responses emerge or the *Gestalt* integration goes on at a simpler level.

#### METHOD OF STUDY AND MATERIAL

There is, of course, nothing specific in the test forms presented for the patients to copy. The value of such a study lies not in any particular tests, but in the analysis of a series of cases on the same or similar tests with certain principles in mind. It is probably important that the tests should be simple and meaningless. There should, of course, be data as to normal reactions on the same tests. For this purpose the same test forms were used as in the previous study on normal, defective and schizophrenic persons, except that the series was introduced with figure *A* which was found to be more readily understood than the former introductory figure 1. In the majority of cases (except case 1 in this study) figures

9 and 10 were no longer used. It will be recalled that the test figures, except the new figure *A*, were adopted from Wertheimer,<sup>14</sup> who discussed rather exhaustively the principles of perception of these *Gestalten* when they are presented to normal adults. Attention must again be called to the obvious but important fact that, unlike Wertheimer, I am not dealing with simple optic perception. The patients, untrained psychologically, are not asked to describe their perceptions, but to copy naïvely the forms presented. Consequently the pattern is a visuomotor one. The so-called sensory aphasia, however, is never purely sensory, and paraphasia is certainly a sensorimotor or acousticomotor disturbance. It is questionable whether there is ever a pure function of sensibility without some motor expression. Therefore such a drawing test is not an inappropriate way of testing an integrated function the disturbance of which finds its expression in both the sensory and

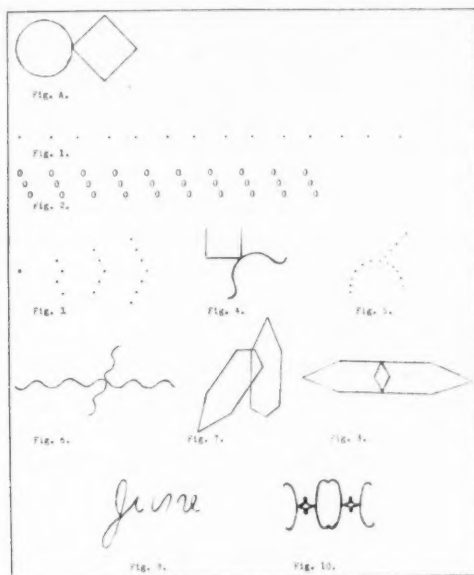


Chart 1.—Gestalt test forms.

motor spheres. Lashley<sup>4</sup> claimed that specific cerebral functions are not disturbed by localized lesions of the brain but that there is a reduction in general efficiency of performance in proportion to the extent of the injury, independent of its locus, with the most highly integrated functions showing the first or greatest disturbance. It is still a question whether such a general statement can be proved to apply to the human brain. However, there is no question but that the so-called sensory aphasia is not a disturbance in speech alone but is associated with disturbances in general behavior, in social adjustment, in thought processes and with more or less motor and apraxic disturbances. The cases chosen for this study were not all examples of pure sensory aphasia, but included cases in which sensory aphasia was one of the outstanding symptoms. The intention has been to study the *Gestalten* in the visuomotor patterns in relation to the existing aphasic disturbance and the tendency for the *Gestalt* function to return to its normal level as the symptoms of sensory aphasia disappeared. The following series of patients was studied in the Psychiatric Division of Bellevue Hospital.

## REPORT OF CASES

CASE 1.—A man, aged 65, was admitted to the hospital at the request of neighbors, who asserted that he had no one to look after him, had become "irrational" two days previously, and was no longer able to care for himself. He was found to have senile arteriosclerosis with a slight right hemiparesis, shown by an increase in tendon reflexes on the right and a slight homonymous hemianopia. He was somewhat cataleptic and showed some abnormal associated movements, such as pulling back the head with opening and closing of the eyes. He did not imitate movements or understand gestures; he did not withdraw from painful stimuli, and the blinking reflex was absent. He was apraxic and his power of attention was poor. He could obey simple commands, repeat simple phrases and count, but would readily become confused with more complicated material. He perseverated a great deal and was paraphasic in all spontaneous speech. Thus when asked: "What is your name?" he responded "Joe—Joe—Henry—Henry—Joe—That's my name, ain't it? Joe." "Where do you live?" "Joe—Henry—downtown—that's where I belong—I belong to Joe." He could not write his name or any meaningful letters.

On the day after admission he was given the test material to copy. The results are shown in chart 2. This is an excellent example of the most simplified method of expressing the outstanding configurational principle in the test material. It is clear that he understood what was wanted, and in nearly every instance (he failed entirely in figure 3) he succeeded in expressing the most important *Gestalt* principle involved in each form in a symbolic way with the least expenditure of energy. He has used the primitive round loop as his symbol for each unit in the organized whole. In figure 1 he has two such side by side (or a little overlapping); the one to the left is a more definite circle than the one on the right—or more significantly, the one to the right is the less perfect circular loop. In figure 1 he has used a series of such units in the proper sequence suggested by the series of dots. Figure 2 is less complete than the rest of his efforts, but it is a relatively laborious test, and throughout his productions one sees the tendency to express relationship with the least expenditure of effort. Here he has apparently attempted to express a slanting relationship of the three unit groups. In figure 3 he has been satisfied to indicate that there is a form present and represents the whole as one unit. This is apparently the most difficult *Gestalt* in the whole series; at least it proves most difficult for growing children. In any case he has shown that the form as a whole stands out against the background, and this, as Koffka<sup>6</sup> has pointed out, is the first principle of *Gestalt* integration. In figure 4 he has recognized and symbolized the two parts of the *Gestalt* and their proper relationship to each other. Figure 5 is an excellent and obvious representation of the circular unit with the upper right-hand dash. In figure 6 the sinusoidal curve line is represented as a series of overlapping loops. The overlapping may also represent the crossing. Figure 7 again shows the two loops in proper relationship to each other. Figure 8 is remarkable because this *Gestalt* was constructed by Wertheimer as a *Gestalt* related to figure 7, with the same two units overlapping in a different way, but it is not recognized in this way by the usual normal person. That it was so recognized and represented by this patient is evident. He has flattened his loops in figure 8 on the horizontal plane to make clear the difference between it and figure 7. Figure 9 is also remarkable. The *Gestalt* is made of two loop units, the first one slightly modified to resemble a J. By the simple use of three loops he has closely approximated figure 10.

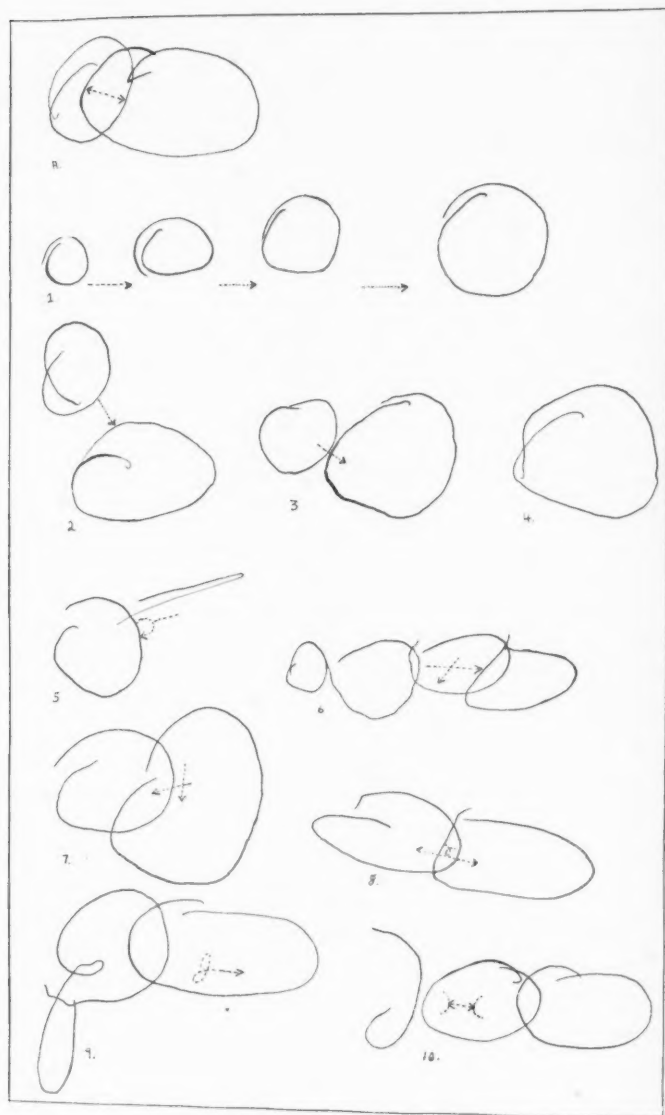


Chart 2.—Gestalt test in case 1.

*Comment.*—In this man, with an organic brain disease apparently due to a hemorrhage in the left temporoparietal lobe, together with the severe disturbances in the more highly integrated functions of speech, thought processes and social and personal habits, there has been a disintegration of the more intricate, internal, detailed organization in these simple sensory (visual) motor patterns. In each instance, however, the outstanding principle of the *Gestalt* as a whole has persisted, and it has often been exaggerated. The patient's interpretation has been an adequate symbolization in which the essential configuration has been recognized. The symbol unit has been the simple, primitive, enclosed, compact loop, which represents the *Gestalt* on its indifferent background.

CASE 2.—This case is more remarkable because the rapid improvement from a state of severe aphasia following a cerebral embolism was followed with the test material from day to day. The patient, a man, a leather worker by trade, aged 43, was admitted to the medical service of Bellevue Hospital on July 12, complaining of generalized edema, dyspnea, nocturia and hemoptysis. His blood pressure was 170 systolic and 116 diastolic, and a diagnosis was made of cardiac decomposition on the basis of hypertension associated with coronary thrombosis. At that time there were no mental or neurologic disturbances. He was given digitalis and other symptomatic treatment and improved rapidly until the night of July 25, when he was reported by the nurse to be acting in a peculiar manner. On examination he was found to have a right facial paresis and to be aphasic. He was transferred to the psychiatric division on July 27. Examination there showed a slight paresis of the right side of the face and the right arm; the latter was apparent from a sinking of the right arm when the two arms were outstretched, but there was no demonstrable difference in the tendon reflexes. There was no hemianopia. There was an exaggerated reaction to painful stimuli, as well as many apraxic phenomena, which were more marked in the right arm than in the left. Movements of the right arm called forth associated movements in the left; less often the reverse occurred. There was difficulty in pointing across the body to any member of the opposite side; for instance, he could not point to the left ear with the right hand, although he could immediately point to the right ear with the right hand and the left ear with the left hand. The patient tended to imitate or otherwise execute any initial movement correctly, but thereafter he perseverated the same movement in response to all subsequent movements or commands until he finally became confused and blocked. On request, for instance, he correctly imitated the movements of turning a coffee-grinding machine; but immediately afterward, when he was asked to point to his right ear with the right hand and the movement was shown to him by example, he responded again with the movement of turning the grinding machine, then became confused and gave up the effort. He was always amiable and attempted to speak; he repeated the command, however, several times before responding and then had difficulties in choosing his words. He often hit on the wrong word and perseverated this until confused and blocked. For example, when asked: "What is the matter with you?" he responded, "Well, sir, a few days before I came I had a—a—a strawberry festival—well, I had a festival—like a festival—a festival—." His efforts to copy the *Gestalt* tests showed similar phenomena. He had an apparent understanding of the problem and an initial correct response, well organized and executed, but this response tended rapidly to perseverate itself until his production became completely disorganized or "deteriorated," and his intellectual efforts were finally paralyzed. The test was repeated daily from the fifth day after the cerebral embolism until the twelfth day, when he had made a marked improvement and

was taken home by relatives in a condition in which he was again able to care for his own needs and carry on an intelligible conversation without mental confusion or paraphasic mistakes. He still seemed somewhat euphoric, however, and uncertain of himself.

Chart 3 shows five daily productions. On July 29, on the fifth day after the cerebral accident, he made a good effort to reproduce figure *A*, making a satisfactory circle and showing the proper relation between the circle and the square, but he was less certain of the details of the square. Dissatisfied with the results, he tried again, but did even worse the second time, when the circle was less well executed and the square was placed inside of it. Actually the square took the form of a 4, because he looked at his own first production, mistook it, and said, "Oh it is a four." Now in attempting figure 1 he perseverated his own original loop, but he interpreted the *Gestalt* concept or sequence of units from the test form. In attempting figure 2 he merely perseverated his previous response. In observing figure 4 (which was presented to him after figure 2) he may have noted a resemblance to his own 4 in figure *A*; for a while he perseverated this, but rapidly confused it with his former loop perseverations. When figure 3 was offered to him he again perseverated his previous response until all evidence of *Gestalt* or organization was lost in a trailing line. When encouraged to try again he only repeated the tail end of the trailing line and then gave up the test in confusion. In the beginning of the test there appears an attempt to write his own name, which began correctly with the initial C, but ended in a meaningless scribble. This tendency to scribble, as shown both in his name and in the latter part of the test figures, may be a reversion to the stage of scribbling seen in small children and low grade defectives, a stage preceding that in which evidences of *Gestalt* organization appear.

On the next day, figure *A* was reproduced with better confidence and execution. The only mistake, the failure to orient the square on the diagonal, is a more primitive response; it was corrected on the next day. Figure 1 on this second test was produced by a perseveration of the last part of figure *A*, the square. The idea of a horizontal sequence was represented with the square as the symbol unit. The same tendency is even more evident in figure 2, where he produced three horizontal sequences of squares. This tendency to interpret figure 2 as three horizontal lines was shown to be the more primitive reaction in the mental defectives of my previous study,<sup>1</sup> and only in the higher levels were the vertically slanting groups of three loops recognized as the unit of the *Gestalt*. The tendency for compactness, closure of open spaces, condensation of the *Gestalt* as a whole and the resulting conservation of energy appears clearly in this case as in case 1, but it finds a different mode of expression. Figure 4 was offered next, and it will be seen that by modifying his square unit symbol to the extent of omitting the top line of his square he produced the first part of the test figure; he then tended to perseverate his previous production with increasingly poor execution until he finally gave up the test in confusion and dissatisfaction. Definite progress, however, was made on this second day; interestingly enough, the progress was in the organization of the *Gestalt* as a whole rather than in the details. The patient eventually failed because of his uninhibited tendency to perseverate the same details until he was unable to adapt them to the test pattern. Then he became dissatisfied, confused and blocked.

On the seventh day he executed figure *A* correctly. He then attempted figure 1 as a new problem and showed that he was aware of the problem. Each little indentation in the horizontal line was a representation of the sequence of dots. In the motor pattern this was more evident because he stopped momentarily at each

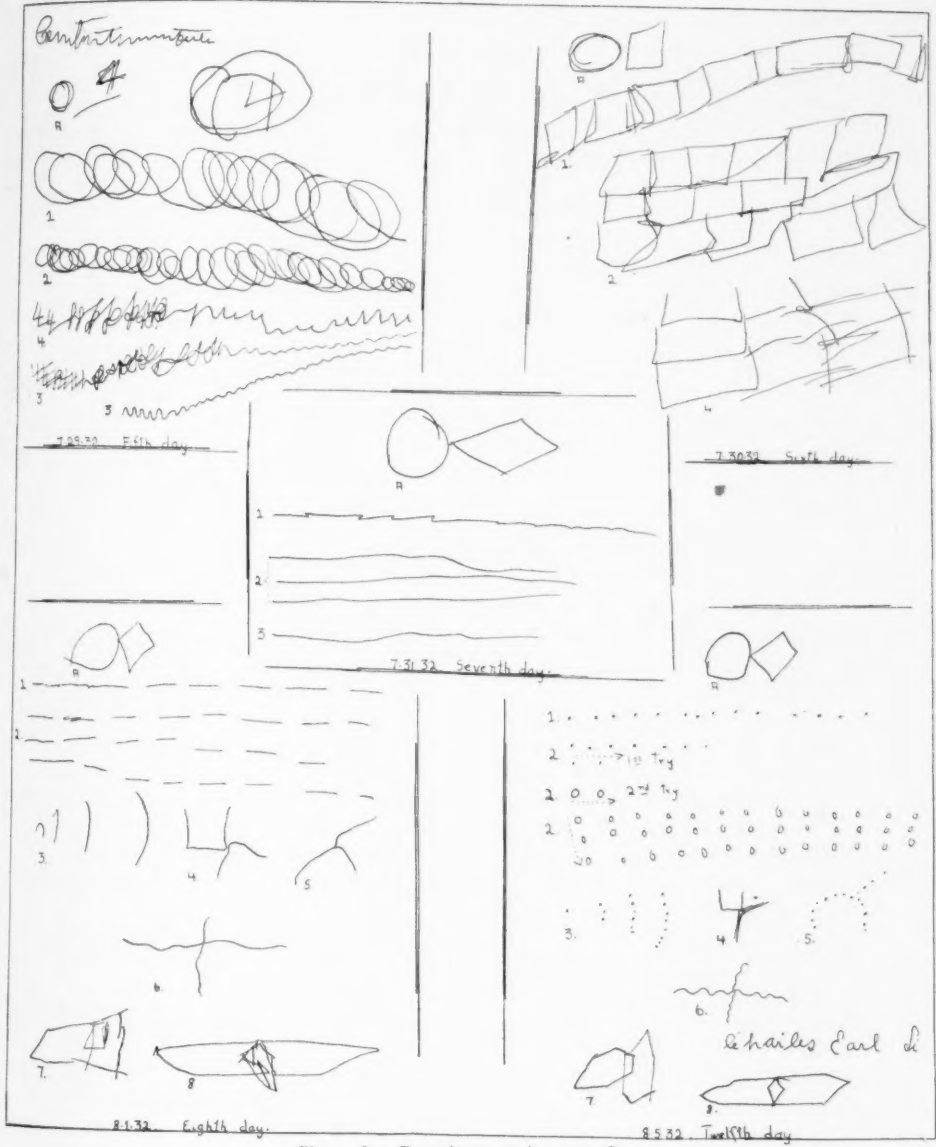


Chart 3.—Gestalt tests in case 2.

indentation. At the end of the line the indentations are less evident, but they were also marked by pauses as he performed the test. Figure 2 was performed in the same way as the three parallel forms of figure 1. With figure 3 he started in the same way, became completely confused and gave up the test.

On the eighth day, figure *A* was correctly formed. Figure 1 was this time broken into interrupted lines; before, he had merely interrupted his movements in the construction of a continuous line. Figure 2 was again drawn as three parallel forms of figure 1. Figure 3 was now attempted, and the main principles of the *Gestalt* were represented by horizontal lines. Figure 4 was fairly well done. Figure 5, like figure 3, was represented by continuous lines. Figure 6 shows the essential organization of the *Gestalt*. Figures 7 and 8, however, were both looked on as composed of three figures in horizontal series, as a result, possibly, of his previous experience with horizontal series in figures *A*, 1, 2, 3 and 4. This day's record shows great improvement, mainly through his increasing ability to inhibit the perseverating influence of the immediately preceding response.

Between the eighth and twelfth days little new was accomplished. But on the twelfth day he reached that point in the learning (or relearning) curve, emphasized by Yerkes<sup>20</sup> and Koehler<sup>21</sup> in apes as well as in man, which is due to sudden insight into the problem as a whole. Figure *A*, as usual, was well done. Figure 1 was shown properly as a sequence of dots. In approaching figure 2 he showed his usual tendency merely to repeat the structure of figure 1; then he suddenly said, "Oh no—it is round holes." Thereon he started his usual horizontal sequence of "round holes"; he again stopped and said, "Oh no—it is three round holes." He at once produced this *Gestalt* in a normal way. He hesitated a minute with figure 3 saying, "It is dots." Then he rapidly produced this in the correct way and continued with the rest of the test with confidence. At the end of the test he laid down his pencil with a sigh of relief saying, "Well, now it is all right, isn't it? Can I go home?" At this time he was also able to write his name correctly (to avoid identification the end of the name is not reproduced).

*Comment.*—It is of no small interest to follow the course in this case of aphasia; in motor behavior, verbal speech and visuomotor patterns (copying of *Gestalt*) the patient showed the same tendency to understand the problem and approach it in a well organized attempt, which was, however, soon frustrated by an uninhibited tendency to perseverate the units of his own response. The rôle of *Gestalt* in the organism-as-a-whole was clear. The outstanding features in the response were: (1) The larger principles in the organization of the *Gestalt* were more significant and persistent than the details, and were often exaggerated; (2) there was a tendency to revert to more primitive reactions such as are seen in children and mental defectives; (3) there was a tendency for more compact, enclosed, energy-saving responses than the stimuli suggest; (4) there was a tendency to use unit symbols influenced by the preceding principles and to represent relationships within the *Gestalt* as a whole by these; (5) there was a marked tendency to uninhibited perseveration (*a*) of the unit symbol, (*b*) of the preceding responses or (*c*) of the principles of the organization, and this tendency was likely to lead to confusion and finally complete blocking or paralysis; (6) recovery from the cerebral insult showed the same type of progressive integrative maturation.

20. Yerkes, R. M.: *The Mental Life of Monkeys and Apes*, Behavior Monograph No. 3, New York, Harcourt, Brace and Company, 1916.

21. Koehler, W.: *The Mentality of Apes*, New York, Harcourt, Brace and Company, 1924.

tion, with episodes of sudden insight into the problem as a whole which is shown in normal developing and learning in human beings and anthropoids; (7) in this recovery or relearning, the larger principles of the relationships of the *Gestalt* appeared before the details of quality of form and distances of space, or in Wertheimer's terms, of proximity and similarity.

CASE 3 (chart 4).—This is another example of an aphasic person who reacts by expressing the total organization in the correct way with simplified symbols and tends to perseverate from one figure into the next. The perseveration is the factor most responsible for failure to perform the test intelligently, that is, in the most highly organized way.

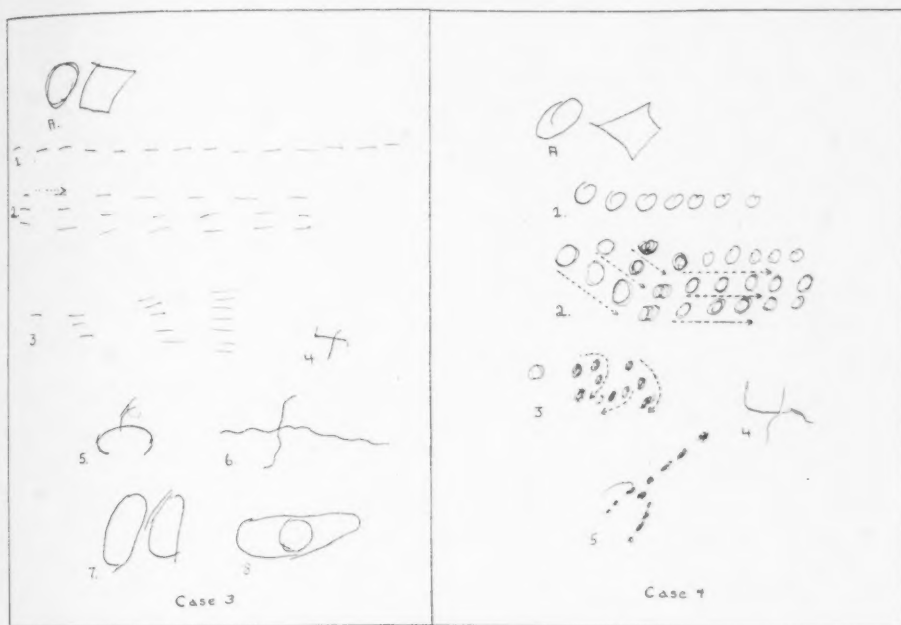


Chart 4.—Gestalt tests in cases 3 and 4.

A woman, aged 50 or more years, was brought to the hospital at the request of neighbors who stated that, two days before, while talking to one of them she suddenly had a peculiar stare in her eyes and twitching of the face and began talking in a funny way. After that she was said to have remained "irrational" and was no longer able to care for herself. On examination she was found to have hypertensive heart disease with arteriosclerosis. The Wassermann reaction of the blood and spinal fluid was negative, but the spinal fluid contained fresh red blood cells on the day of admission and was xanthochromic five days later. The patient was dull and drowsy, though amiable when aroused. There was a tendency to catalepsy in the arms. She did not react to painful stimuli or show any defensive mechanism, even the blinking reflex. She was apraxic and awkward in handling objects; she was likely to hurt herself with a knife or a burning match if either was given to her. She spoke with paraphasic mistakes, was irrelevant and often perseverated. When asked, "What color is green?" she

said, "Well, I have always had it—all the—my head hurts something awful—awful—all the time." She could not name objects or name her own fingers. She improved so that within a month, though she continued dull and irresponsible, her speech was nearly normal. Recovery in the beginning was too rapid to show the various stages in the return of the perceptual motor *Gestalten*. On the fourth day after admission, she did not seem to understand the problem and did not respond to the test at all. On the fifth day she responded with the productions in chart 4. At this time she could write her own name, with some tendency to perseveration of letters and parts of letters. The *Gestalt* productions showed nothing not already described in the previous case, but confirmed many of the findings earlier discussed. The *Gestalt* tendencies were again expressed in the simplest way. In figure 1, the principle of the horizontal sequence appeared, and the same production was carried over again into figure 2. The subsequent figures were also produced in the simplest possible way to show the implied relationships. The tendency to use simple compact loop units was also seen.

CASE 4.—This shows a more striking tendency to utilize the loop as the unit symbol to express the recognized organization of the *Gestalten*; repeated failures arose, however, from the tendency for uninhibited perseveration from the preceding figure.

The patient, a woman, aged 38, was said to have been a dependable waitress in a large hotel for twelve years. One morning she did not report to work and was found in a dazed state, unable to give an account of herself. On examination it was discovered that she had uremia; the condition progressed and resulted in death three weeks later. Following admission to the hospital, she was euphoric, restless, perplexed, incoherent and perseverating; from time to time, however, she made pertinent remarks, such as, "The left side of my face is jumpy. Why does my hand keep going down? Something happened to me in my room—my bath room—my bath tub. I don't know what I am saying. I am all mixed up. I have a terrible headache. I can't remember words." There were twitchings in the left side of the face and weakness of the right hand. She reacted promptly to pain. She showed some finger agnosia, often failing to name her fingers or to show the correct one; she also failed to point to other parts of her body correctly. She had apraxic symptoms and attempted, for instance, to write with the wrong end of the pencil. She made mistakes even in writing her own name and address. She also made mistakes in copying, in reading letters or numbers and in naming objects. She often perseverated with the same wrong name from one object to the next. She frequently failed to obey simple commands or to answer simple questions. She could not add, subtract or multiply, even with such simple problems as "three times four" or "twelve minus seven." She showed some memory defects; she could not repeat three digits. On the day after admission, she produced the figures shown in chart 4. Figure A was satisfactory. Figure 1 was started like figure A except that the loops were smaller. The idea of the sequence was followed out with the loops. Figure 2 was at first attempted in the right way, using the same loop unit and arranging the first in a vertical slant of three, but this arrangement was soon given up for the horizontal sequence pattern of the preceding figure. Figure 3 was started with the same original loop; the second unit of the *Gestalt* was bravely attempted, but the last part of the *Gestalt* ended in confusion. Figure 4 was simpler for this patient. Figure 5, apparently influenced by the previous figure, was started in the wrong way but completed well. There were apparent here both primitive influences and more highly organized endeavors. The efforts quickly led to fatigue, so that the patient soon gave up the test. There

was essentially a tendency to return to the nonorganized flux from which the optic field gradually becomes organized into *Gestalten*.

Similar tendencies are seen in chart 5, which shows part of the productions in case 5. At first one is inclined to think that the productions are meaningless and without principle, organization or relation to the forms offered for copy, but they justify a more careful study.

CASE 5.—The patient, a woman, probably aged 60 or 65, had been found wandering on the street without identification and entirely unable to communicate with the examiner. Her only form of speech was a grunt. In the hospital she was amiable and cooperative, but perplexed and constantly watching the windows

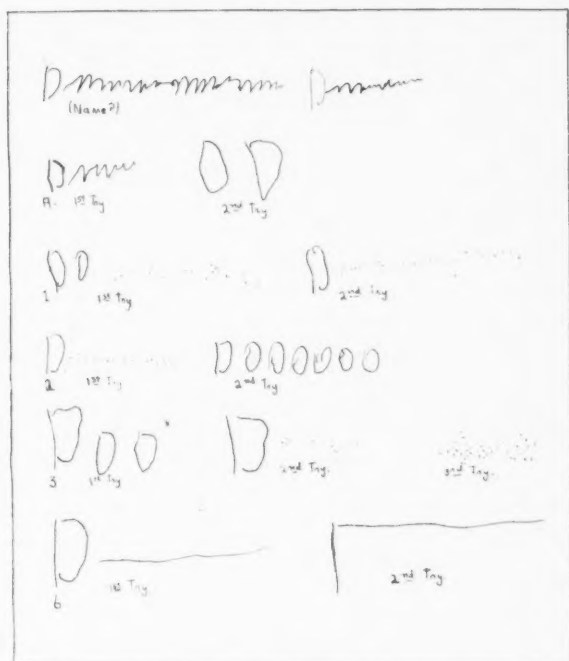


Chart 5.—Gestalt test in case 5.

and doors as though expecting someone. She was senile, with arteriosclerosis and a blood pressure of 140 systolic and 80 diastolic, a shuffling gait and a tendency to drag the left foot; there was a discontinuous ankle clonus and a positive Babinski sign on the left. For the first few days her condition seemed to fail. She was unable to care for her personal needs and required spoon feeding and nursing care; swallowing became difficult, but she again improved until at the end of three weeks she showed no neurologic deviation and was in fair physical condition. Although she seemed more alert mentally and made every effort to understand others and to express herself, the aphasia did not improve. She could obey a few simple commands, such as "stand up" and "sit down," could care for her own personal needs and find her way about the ward. She had some apraxic symptoms, such as trying to erase with the end of a pen. When given paper and pencil her spontaneous productions were always a scribble similar to that at the top of the

plate. It is possibly an effort to write her name, and the initial form may be the letter D; in chart 3 of case 2 and chart 6 of case 6 the initial form is the first letter of the name. This particular initial form, however, is not far removed from the primitive loop unit symbol. The patient's scribble, as in the previous case, is like that of young children and low grade defectives. When figure A was offered her she began her usual pattern, but in some way inhibited the continuous perseveration of the scribble. Asked to try it a second time, she drew two of her initial figures in a relationship suggested by figure A. When figure 1 was offered to her, she repeated her previous production but followed it by a series of irregularly placed dots. Encouraged to try this figure a second time, she again drew a single initial figure and followed it by more uniformly placed dots. When figure 2 was offered her she again repeated her previous performance, but on the second effort she made a series of loops beginning like her own initial figure but gradually becoming more like the simple, primitive loop. Similar tendencies were seen in low grade defectives who were just able to express the relationships in the *Gestalten*.<sup>1</sup> When figure 3 was offered, she again reproduced her previous performance, and on the second trial started with her initial figure and followed it by dots such as she had used in figure 1; on the third trial by omitting her initial figure and scattering her dots she produced a figure not dissimilar to the test figure 3. Many of her productions have been omitted, but in figure 6 it is seen that she again used her initial figure followed by a horizontal line (the basic principle of the test figure). In a second effort she used only the vertical arm of her initial figure, followed—rather than crossed—by the horizontal component of the figure. This difficulty in crossing lines is a primitive as well as a pathologic tendency and apparent not only in the optic<sup>1</sup> but also in the tactile field.<sup>8</sup>

*Comment.*—Thus this patient, who had lost all power of oral or written language, but who was still able in some way to understand the situation, to care for her simple personal needs and to understand the test problem sufficiently to cooperate with it, showed a tendency to use an initial form figure, a characteristic unit symbol derived from a loop form and possibly modified by her own name initial. In copying the *Gestalten* she tended to use this initial form figure and to follow it by some production suggested by the test figure. She rarely accomplished a satisfactory result on her first trial, however, and she experimented a good deal as children experiment with various forms and designs until they hit on one that fits their meaning.<sup>2</sup> Her repeated efforts usually consisted in efforts to inhibit the influence of her previous production or of her own initial form or unit symbol. Other primitive tendencies, such as perseverations, recurrence of loop formations and inability to cross lines, were also in evidence. She was easily exhausted and discouraged by her failures, and thus unable to continue the test.

CASE 6 (chart 6).—This patient showed some rather severe apraxic symptoms as well as some motor disability in the right hand owing to a mild right hemiparesis. His productions are interesting, however, especially because of his tendency to perseverate his own mistakes and finally arrive at a paralyzing confusion as in case 2. His errors usually arose from misinterpreting a series of dots as writing of some sort. In the other *Gestalten*, in which the organization was on a broader principle, he showed a remarkable capacity to grasp and reproduce the *Gestalt* principles in spite of his rather severe aphasia and motor disability.

The patient, a man, aged 60, was a dishwasher who suddenly collapsed over the dishwashing machine and was unable to talk. At the hospital we found him to be senile with the usual deteriorative and arteriosclerotic changes. The retinal vessels were sclerosed. Further, he had a right facial weakness, weakness of the

right arm, causing clumsiness and tremulousness of all movements, and a distressing numbness. He was insensitive to pain, especially in the right arm. He was amiable and cooperative, but apathetic and bewildered. Although he was awkward and slow, he was able to care for his personal needs. His speech was unintelligible, but he understood a few simple commands and imitated a few simple movements. He could not scratch a match; he dropped it and did not know that he had done so.

When offered the test material on the eighth day after the cerebral accident, he had difficulty in handling the pencil and was awkward and slow. Still he produced figure *A* fairly well, although the square was not diagonally oriented, and the circle was produced only by a number of small segments. When figure 1 was offered him, however, he repeated the last part of his previous performance,

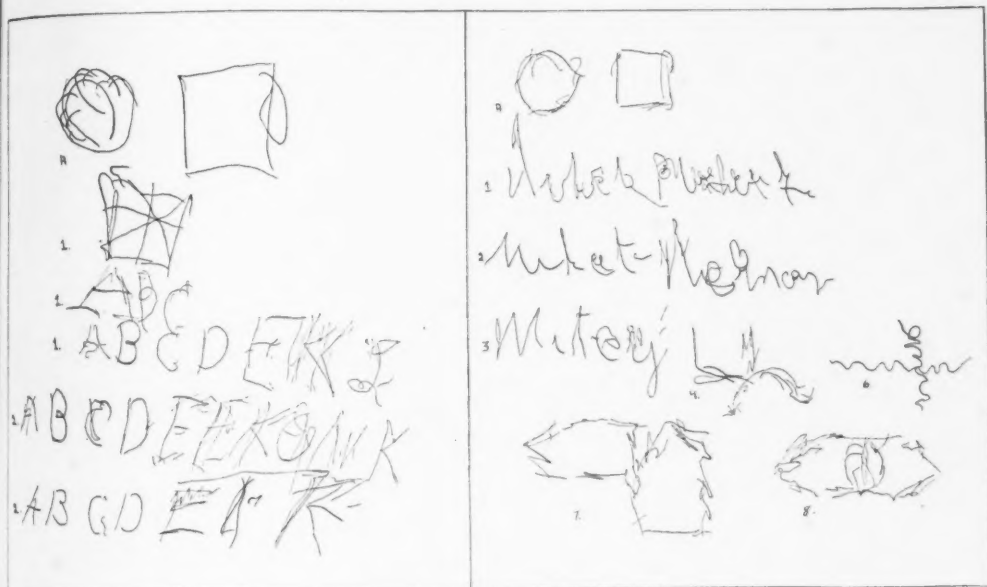


Chart 6.—Gestalt tests in case 6.

the square. On seeing that this was wrong, he drew lines through it; getting the idea of a capital A from this and the concept of sequence from the test figure 1, he started the ABC's. After he produced the first three letters, an effort was made to divert him and start him again on the copying, but he persisted in writing the alphabet. This time he continued until he became confused. When offered figure 2, he repeated the same performance on both the first and second trials. Each time he lost the sequence as well as the ability to form the letters accurately just at the letter E. This block was not due to fatigue, for he was able at once to start again and to execute the first part of the series better on each succeeding trial.

Two days later, when he seemed more alert and somewhat improved, he was offered the test again. Figure *A* was produced about as before, although with somewhat better motor facility. Figure 1 called forth an attempt at sequential writing; it was an almost unintelligible scribble, although the initial letters each

appeared to be the letter W, the first letter of his name. Figure 2 and the figures made up of a sequence of dots, namely, figures 3 and 5, called forth the same response. But the other figures (4, 6, 7 and 8) were well organized *Gestalten*; the lines, however, were broken and irregular because of the motor disability. These productions show that the larger principles of organized *Gestalten* may be retained while the finer principles involving the sequence of dots and small circles call forth other forms of organized sequence; the other forms were here, in one instance the alphabet, suggested by a self-performed error, and, in another instance, a primitive scribble which was perhaps an effort to write his own name.

Case 7.—A man, aged 59, had aphasia and left hemiplegia on the basis of cerebral arteriosclerosis. The patient always had been left-handed. He had a

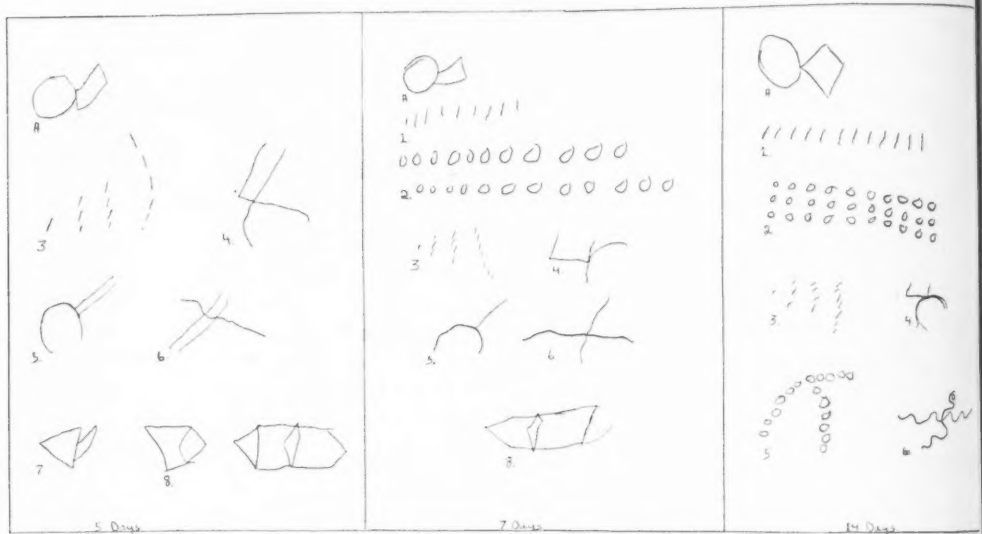


Chart 7.—Gestalt tests in case 7.

left external strabismus. Aphasia tests showed that spontaneous speech was paraphasic and perseverative. He obeyed simple commands poorly; he could not repeat series of numbers or names, nor could he read or write to dictation. He had a finger agnosia. His perception of pain was poor. He tended to be euphoric, but readily broke into tears. He showed no apraxic symptoms. He was restless at night and needed supervision in his personal care. He talked constantly, and realized that something was the matter with his speech, but always pointed to his teeth, which were in poor condition, as the cause of his difficulty. When asked to draw the picture of a man, he did so very poorly, and then said: "That is supposed to be a lady. I can't suppose very good, but that is what it is—supposed to be a lady. That makes the ladies children—for instance, a lady like you—that makes the children. Still I would work you know—and show where it is and say it is all right. It is my teeth. After I used to be able to work and could work, but after my feet got this way—it got this way. I could show you right from the start." His conversation always went in the same way. However he started, he

would make some incoherent remarks about children, then try to explain his present disability, explain that his teeth interfered with his speech, insist that he could work and ask that he be given a chance to do so.

The same perseverative tendencies were seen in his *Gestalt* productions (chart 7). When the tests were given five days after admission, parallel oblique lines tended to perseverate in figures A, 4, 5, 6 and 7. Figures A and 5 were remarkably alike, and so were figures 4 and 6. The first attempt to make figure 8 resulted in a *Gestalt* similar to the preceding figure 7. The patient showed a rapid improvement in clinical symptoms, and two days after these tests was able already to inhibit the tendency to perseverate and showed an ability to individualize each figure instead of producing the second figure as a variation of the preceding one.

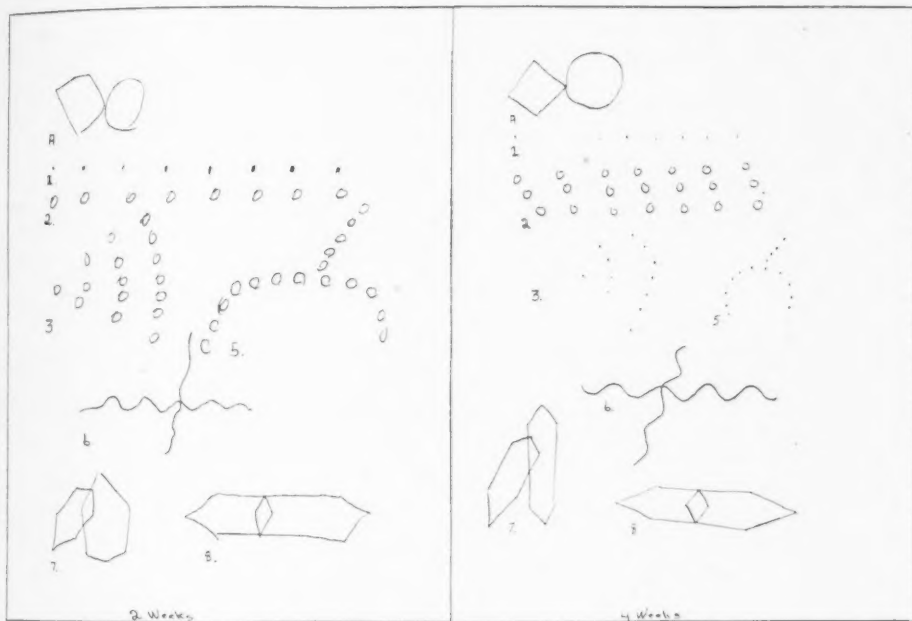


Chart 8.—Gestalt tests in case 8.

A week later, his productions were probably about normal for his intellectual level. A right-sided cortical lesion in this case was productive of a disturbance in the *Gestalten* with aphasia because the individual was left handed.

Case 8.—This case is of interest because of some knowledge of the localization and extent of the lesion which produced a sensory aphasia with relatively little disturbance in the perceptual-motor *Gestalt* functions as shown by the copying of these test forms.

The patient, a man, aged 27, had had one year of college education. While under the influence of alcohol at a party he fell over the bannister to the floor below, alighting on his head. He was brought to the hospital in a stuporous condition which persisted for several days. Roentgen examination showed multiple fractures of the vault of the skull on both sides. There was a bilateral Babinski reaction, and on the fourth day there developed right-sided convulsions with

paralysis of the right side of the body, including the face. A diagnosis of laceration and hemorrhage in the left motor region was made, and five days after the accident he underwent a decompression operation in the left frontal parietal region, which revealed laceration and maceration of the underlying brain, subdural multiple hematoma and intraparenchymal hemorrhages. Dural vessels were tied; part of the dura was cut out, and free blood, blood clots and macerated brain tissue were removed. The remaining brain looked blue and contained many hemorrhagic areas. The patient improved immediately, however, and in a few days there was no right hemiparesis, recurrence of convulsions or other neurologic deviations. As he began to speak, he showed a severe sensory aphasia with the following features: He was restless, especially at night, and noisy, but always euphoric, with some manic behavior. He talked continually in a facetious strain with many paraphasic mistakes. He was unable to name objects and showed a finger agnosia. He had difficulty in understanding any commands or questions, whether spoken or written. He also made paraphasic mistakes in writing. When asked to count to 10 he said: "one—two—three—any G— d— thing. All right, who can't count to ten? I would do it—any one could. Two—it must be very—. Same G— d— thing. Where did you get that nice one (referring to the stenographer)?" He wrote a letter to his mother: "Dear mother—I am wanting meeting. I am myself leaving meetings. I am feeling fine." Although still somewhat euphoric and paraphasic in talking and writing, he went home much improved at the end of a month.

His productions in copying the figures are seen in chart 8, two weeks after the accident when he still showed a severe aphasic disturbance, and one month after the accident when he was much improved. The remarkable thing about this case is that the disturbance in *Gestalt* integration was so slight in view of the gross cortical lesion in the left frontal parietal region and the rather marked sensory aphasia. Considering the extent of the lesion, however, it is also of interest that there was such a marked improvement from the aphasic disturbance.

Even two weeks after the accident, when the aphasia was still severe, the *Gestalt* productions might be considered nearly normal if it were not for the fact that the patient was of high intelligence and had had a year of college work, which included some mechanical drawing. The productions two weeks later were entirely normal from any standard, and in comparison with these the earlier productions show features of a lower level of intellectual integration. The work as a whole was done with less precision; figure 2 was produced by a single horizontal row, and figures 3 and 5 with loops instead of dots, while the angulation in figure 3 was not well shown. All of these features, however, were corrected in the later productions.

#### SUMMARY AND COMMENT

In studying the *Gestalt* function in visuomotor patterns by means of copied form in eight cases of organic brain disease in which sensory aphasia was a conspicuous symptom, the following observations were made:

Case 1 showed a disintegration of the more intricate, internal, detailed organization of the *Gestalten*, with a perseveration of the fundamental, outstanding *Gestalt* principle by the use of the primitive loop as the unit symbol. Nothing of the building stones of perception but only

the intricacies of the higher integrative capacities were lost by the cerebral lesion; the organism-as-a-whole continued to respond at a more primitive level by establishing a new equilibrium between the test forms and the mental symbols of the more primitively functioning nervous system.

Case 2, which we followed day by day through the course of recovery from sensory aphasia, showed the following tendencies in visuomotor responses: (1) perseveration of the larger principles of *Gestalt*; (2) emergence of primitive responses; (3) utilization of the compact, enclosed, energy-saving unit symbols to show relationships; (4) perseverative tendencies that led to confusion and blocking; (5) recovery accompanied by progressive integrative maturation with sudden episodes of insight. This case shows that the external object, in this case the test forms, is not the only factor in perception, but that the external and the internal situations play a large rôle. The external situation includes other objects in the field, both in time and space. In these experiments, the preceding test forms frequently modified the response to subsequent forms. Time is as important a factor as space in optic perception; as Katz<sup>22</sup> has shown, and as I have also shown,<sup>1</sup> movement is the first element in perception. Kanner and Schilder<sup>23</sup> have shown that movement is always present in optic imagery.

Perseveration arises more from temporal than from spatial factors and may in some way be compared to the after-effects in sensibility experiments.<sup>24</sup> Thus one *Gestalt* is modified by the previous one if the after-effects or temporal perseverations have not yet subsided or been inhibited.

Case 3 tended to confirm some of the findings in cases 1 and 2. The simple compact unit symbol is used to show the implied configuration.

Case 4 showed similar tendencies with perseverations that led to confusion.

Case 5 showed the usual primitive type of response with the use of the initial of the name, or at least of some individual characteristic of the patient as a modifying feature of the unit symbol. The tendency to retain the initial of the name when all other arbitrary symbols were lost is also seen in cases 2 and 6.

Case 6 showed complicating symptoms of apraxia and motor disturbances. Nevertheless, the fundamental principles in the *Gestalten* are expressed, however laboriously.

22. Katz, D.: Der Aufbau der Tastwelt, Ztschr. f. Psych. **11**:71, 1925.

23. Kanner, L., and Schilder, P.: Movement in Optic Imagery, J Nerv. & Ment. Dis. **72**:489, 1930.

24. Bromberg and Schilder.<sup>8</sup> Bromberg.<sup>9</sup>

Case 7 showed tendencies to perseverate from one figure to the next with a loss of individualization of form when the fundamental principles were still preserved. This occurred with a right cerebral lesion in a left-handed man.

Case 8, that of a man of high intelligence, showed a very slight tendency to a lower level of integration of perceptual motor *Gestalten* following a gross cortical lesion of the left frontal parietal region with a sensory aphasia.

It is generally supposed that in sensory aphasia the first third of the gyrus temporalis primus of the dominant hemisphere is affected. The question arises as to whether such a lesion also produces the disturbances in the visuomotor *Gestalt* function which are described in this paper, or in other words, whether one deals with the same psychologic mechanisms in the *Gestalt* functions as in other symptoms in these cases with sensory aphasia. It is at least possible that the *Gestalt* disturbance is due to a lesion of parts adjacent to Wernicke's area. The disturbance in the *Gestalt* function does not run absolutely parallel to the degree of sensory aphasia. Case 8, with a severe sensory aphasia, showed only a minimal disturbance of the *Gestalt* functions. In this case the lesion seemed to extend from the temporal lobe more in the frontal direction, while in case 1, with a maximal disturbance, there was a slight homonymous right hemianopia, indicating an extension of the lesion toward the occipital pole. In the other cases, the neurologic evidence was not sufficient to determine which parts besides the Wernicke area were affected. In every case but one the symptoms pointed to a lesion in the left hemisphere; the one exception was a right-sided lesion in a left-handed man. One may conclude therefore, in a general way, that the lesion which produces this disturbance in the *Gestalt* function either coincides with the Wernicke location or lies nearer to the occipital pole in the temporo-parietal region. Gelt and Goldstein<sup>12</sup> have reported the case of a patient with a lesion in the occipital region who showed a complete word-blindness and a complete loss of power to recognize the most elementary *Gestalten*, while sensory aphasia in the common sense was absent. In the cases reported here, primitive functions of *Gestalt* not only were preserved, but were even exaggerated. It seems that the *Gestalt* function is more involved the nearer the lesion comes to the occipital region. It is probable that the *Gestalt* function is not strictly identical with the sensory speech mechanism, but merely allied to it. Thus, in a general way, we may conclude that the area most probably involved in disturbances of the visuomotor *Gestalt* function, as exemplified by these copied test forms, is that between the temporal, parietal and occipital lobes of the dominant hemisphere.

Orton<sup>25</sup> has emphasized the different levels of visual function, the simple perceptive level being about the calcarine fissure, while the visual cognitive and associative level surrounds it. The visual motor *Gestalt* function would seem to belong to one of the higher levels, probably the associative.

Speech and *Gestalt* functions are integrative functions of the personality-as-a-whole, with the cerebral cortex as their highest center of integration. Speech is based on symbols arising from the interplay of the stimuli of the external world and the sensory field in any given situation or context. The properties of the sensory field are determined by the laws of its biologic nature which are limited by the maturation level, the integrative integrity (lack of lesion), the status of the personality, including the emotional complexes, and the given situation. Lesions in the higher integrative centers would change the response to a lower integrative level, with the emergence of primitive tendencies which may modify each other in such a way that the response varies from case to case and day to day depending on the total result of all the factors involved. These factors include the basic biologic matrix, the previous maturation level, the integrative level permitted by the specific lesion, the locus of the lesion and the emotional complex of the individual-as-a-whole, and in response to this new experience and the situation-as-a-whole.

These studies of disturbances in perceptual motor *Gestalten* in organic brain disease indicate that the *Gestalt* principles are never fixed, but are the integrative response of the personality-as-a-whole in any given situation; in disintegrating cerebral lesions they tend to revert to more primitive levels, and, as the brain recovers from its insult, they tend to follow the laws of developmental maturation in returning to the higher integrative responses.

25. Orton, S. T.: "Word-Blindness" in School Children, Arch. Neurol. & Psychiat. **14**:581 (Nov.) 1925.

## CLINICAL VARIABLES IN SCHIZOID PERSONALITIES

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The relation between prepsychotic personality and psychotic manifestations has been observed by many writers. Especially in the consideration of the functional psychoses, the affective and schizophrenic disorders, a dichotomy of personality types has been assumed and has led, on the one hand, to the concept of the extroverted, cyclothymic, syntonik personality as associated with the affective psychoses, and, on the other hand, to that of the introverted, schizoid, shut-in type usual in schizophrenic breakdowns. Most writings on the subject fall into the domain of clinical intuition rather than science.

In an attempt to approximate scientific objectivity, a statistical study of prepsychotic personality was initiated at the Boston Psychopathic Hospital in 1928. The justification for such an approach is suggested in the statement of Dorothy Swaine Thomas in an article on "Statistics in Social Research:"<sup>1</sup>

Since experiment will always be difficult to carry out with human materials, we must look to statistics as a method that we shall have to use if we wish to obtain real objectivity. Statistics, however, can never completely exclude other methods of analysis used in sociology. It should always be regarded as a methodological scheme for the objective evaluation of relationships and data that have been previously mulled over.

The aim, therefore, of the research into prepsychotic personality was "the objective evaluation of relationships" which had been described frequently in the literature.

Obviously such a project yields a wealth of material which can be analyzed in many ways, from both a clinical and a methodologic point of view. The present study, which is primarily clinical in nature, is concerned with a small group of cases which were selected from the

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Read at a meeting of the Massachusetts Psychiatric Society, Dec. 21, 1932.

This article is a part of a study of schizophrenia at the Boston Psychopathic Hospital which was made possible by a grant from the Laura Spelman Rockefeller Foundation.

1. Thomas, D. S.: Statistics in Social Research, *Am. J. Sociol.* **24**:1, 1929.

total number included in the research on the basis of a common personality background. This background was arbitrarily defined to include traits that are most commonly considered the core of the schizoid personality. The study was undertaken with two questions in mind: 1. In patients with similar personalities, who are known to have been shy, seclusive, sensitive and close-mouthed (the type of traits which stamp a person as being "different" in the community) is there any similarity in the clinical picture when they break down? 2. Can the schizoid personality be designated by such a constellation of personality traits? In other words, this study is an attempt to determine whether a personality type such as we have assumed exists, and whether persons who have such a personality break down with similar psychoses.

#### METHOD OF STUDY

Cases of the type desired were selected in a fairly objective manner by means of code sheets which had been filled out for each case studied in the research. Of such cases, 327 had been thoroughly investigated during a period of three years, in the following manner: The cases, taken from the general hospital admissions to the Boston Psychopathic Hospital, were selected by two research psychiatrists on the basis of diagnosis and the possibility of securing adequate information from outside informants. Cases of schizophrenia (as well as of paranoia and paranoid conditions) were of chief interest, while cases of manic-depressive psychosis, dementia paralytica and those otherwise suited for control groups were also included. The possibility of securing adequate information implied cases in which a complete history could be obtained, the informants were reasonably intelligent, cooperative and reliable, there was no language difficulty, and parents or close relatives were available to give information about childhood. Cases of patients regularly committed to the hospital for more than the usual ten day observation period were also included if otherwise suitable for research. It must be noted, therefore, that this group was highly selected, as it included for the most part young, fairly intelligent, English-speaking, middle-class patients.

Each patient was examined according to routine hospital procedure. A complete anamnesis was obtained, and physical, psychiatric and psychologic examinations (whenever possible) were made. In addition to the routine study made by the house physician, further examination of each patient was made by the research psychiatrist. As a rule, the patient was also seen during the rounds of the ward and at staff meetings. With the exception of a small group that was studied by the house physician and research psychiatrist only, each case was referred to a research social worker who obtained as complete data as possible pertaining to environmental, developmental and prepsychotic personality factors from parents, siblings, relatives, teachers, employers, physicians, friends, other hospitals and other social agencies.

When the study was completed, the information from all sources was pooled. The data obtained were discussed in conference with the research psychiatrist, physician and social worker present. Each statement was regarded in the light of all information; contradictory evidence was weighed, and the contributions of the different informants were evaluated. In its final form, the information was entered on code sheets prepared for the purpose of insuring the possibility of statistical analysis by some uniform method of tabulation. The code sheets

were supplemented by the hospital record and the social history which attempted to give a complete and dynamic picture of the total personality of the patient and of the molding influences in his life, with a conscious effort to make interpretations only on clearly stated facts.

*Outline for the Study of Personality.*<sup>2</sup>—The largest portion of the code sheet consisted of a personality outline, originally devised by Dr. F. L. Wells and based on schemas heretofore used by various investigators. The outline did not aim to be comprehensive, but rather to provide a few variables which could be reliably studied and objectively determined. The traits included were those which are most frequently discussed in the literature on prepsychotic personality. In designing the outline it was assumed that a single trait could be defined "as one whose varying condition in men can be measured on one scale," and that the distribution for each trait would approximate a normal distribution curve. The deviations in the extremes were of special interest, so that the upper and lower quartile of each trait were defined to denote antithetical characteristics. Provision was made for coding cases in which there were exhibited no extreme deviations in a given trait as average.

A number of traits, however, were coded as either present or absent, such as neurotic habits and excessive day-dreaming. In others, in which one extreme could not practically be separated from the average, the two were combined, leaving one extreme only. The average group for the most part included cases which were not outstanding or which could not be classified in one extreme or the other. It can be assumed, then, that those traits best describe a given case, or distinguish it from others, which are coded in one extreme or the other. For the purpose of the present study, the extreme of each trait which is thought to be most characteristic of patients who become schizophrenic has been called the schizoid trait, while its opposite, which is more likely to be associated with the affective disorders, is called the cycloid trait.

About half of the traits on the outline were described separately for childhood and adult life. Childhood was arbitrarily defined as the period up to, but not including, the age of 16. When the onset of the psychosis had occurred before the age of 16, traits which allowed for coding only in adult life were estimated on the basis of the personality during childhood. Prepsychotic personality was clearly defined to include only that portion of the patient's life which preceded the first indication of any mental disorder as determined in conference by clinical judgment on the basis of all available information.

Definitions of all terms used on the personality outline were formulated with the hope of securing precision and uniformity, since obviously individual interpretations can distort any findings. While many objections can still be raised to this kind of approach (they will be discussed in another research publication), we believe that this study of prepsychotic personality may have suffered less from many of the common errors because it was based largely on behavioristic manifestations, took into consideration the account of more than one observer and attempted to bring in some element of control.

#### DEFINITION OF SCHIZOID PERSONALITIES

The arbitrary criteria which were selected to delineate schizoid personalities were those traits relating to friendships, recreation, reaction to social group, communicativeness and sensitivity. The schizoid

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2. The questionnaire used in the research on which the study was based will be supplied by Dr. Kasanin on request.

extremes of these traits can be said to be the nucleus of the schizoid personality as described in the literature. Patients so coded had in pre-psychotic life few friends, preferred solitary amusements, were shy and followers in the group, were close-mouthed and were extremely sensitive. Among 327 cases, of which 151 were cases of schizophrenia, only 33 were found in which all five of these traits were exhibited. In 16 of these cases, all five traits were described in adult life only, or after the age of 16, whereas in the remaining 17 these characteristics had been present since early childhood. The material presented in the discussion of these cases was obtained from both the case histories and the code sheets. The findings in the cases are described under various headings that are of interest.

#### CLINICAL FINDINGS

*Sex.*—The cases show the same distribution for sex as the total number of cases studied in the research: 18 in females (54.6 per cent) and 15 in males (45.4 per cent) out of a total number of 178 females (54.4 per cent) and 149 males (45.6 per cent).

*Age on Admission.*—The average or mean age on admission was found to be 21.6 years for males and 31.1 years for females. A ten year difference was also observed for the median age, 22 for males and 32 for females, while even a greater difference was true for the mode, 17.5 for males and 35 for females. This difference is striking as compared with the total group in which practically no sex difference in age occurs. Here the mean age is given as 35.8 for males and 37.9 for females; the median falls at 25.3 for males and 25.9 for females, and the mode for both is at 22.5. For some reason it appears that females with the constellation of traits which we have selected tend to be admitted to the hospital later than males. One deduction that may be made is that a constellation of traits such as that outlined is much less acceptable for males than for females in the present state of culture, so that these traits become noticed earlier in the male and a radical decision has to be made much sooner; the female, however, can "drag on" ten years longer without the community or relatives insisting on institutional disposition. Since most of the cases have been diagnosed schizophrenia, as will be shown later, the other possible explanation, which raises a question that we are unable to answer, is that schizophrenia seems to develop later in females than in males.

*Age at First Indication of Any Mental Disorder.*—The question whether the psychosis actually occurs at an earlier age in males may be answered for the present group by a consideration of the age at first indication of any mental disorder as given on the code sheet for both clinical estimate and social criteria. (A sharp distinction was made between clinical estimate and social criteria since it is well known that a person may have odd and peculiar ideas long before his conduct gives objective evidence of mental disorder.) Here the mean age for males is 18 by clinical estimate and 19.2 by social criteria, whereas for females it is given as 22.1 and 23.4. The median shows less of a difference, being given as 17.5 and 18 for males, and 19 and 19.5 for females. The modes for both sexes concur at 17, clinically and socially. It is apparent that while the onset of mental disorder in this group occurs slightly earlier in males than in females, the difference is less striking than when age at admission is taken as a criterion.

*Age at Onset of This Attack.*—The age at onset of the present attack (during which the patient was studied) as given on the code sheet shows again a large difference. For males, the mean age is 20.6 by clinical estimate and 20.9 by social criteria, whereas for females it is 28.2 and 28.6. The median likewise falls at 19 and 20 for males, and at 30 and 29 for females. All modes occur at 17. It can be observed that while the age at first indication of any mental disorder and the age at onset of the present attack differs by about two years for males, for females the difference is about six years. If in each case the present attack had been the first indication of any mental disorder, ages given for both would have been the same. In 11 cases, however, of which 8 were in females, the present attack had been preceded by previous breakdowns. For this reason, the mean age at the time of the present attack is greater for females than for males, of whom most were experiencing the first breakdown.

TABLE 1.—Duration of Present Attack Previous to Admission

Duration	Number of Cases Based on	
	Clinical Estimate	Social Criteria
7 to 31 days.....	5	9
1 to 6 months.....	5	8
7 to 11 months.....	6	5
Over 1 year.....	5	2
Over 2 years.....	10	8
Unknown .....	2	1
	33	33

TABLE 2.—Type of Onset

	Acute	Subacute	Insidious	Unknown	Total
Definite.....	7	4	4	0	15
Indefinite.....	0	1	15	0	16
Unknown.....	0	0	0	2	2
	7	5	19	2	33

*Previous Attacks of Mental Disorder.*—Of the 11 cases in which there had been previous attacks, recovery was judged to have taken place without defect in 7 cases. In 1 case there was some degree of recovery, but the information was vague. In 3 cases only was there an actual deterioration of the personality.

*Duration of Present Attack Previous to Admission.*—The duration of the present attack previous to admission, as judged by clinical and social criteria, is shown in table 1. By clinical estimate almost one half of the cases had persisted for over one year, and almost a third of the cases for over two years. As would be expected, in all cases clinical judgment tends to throw the date of onset further back than do social criteria.

*Character of Onset.*—The type of onset was coded for each case and appears in table 2. Summarizing the findings as to onset, it appears that the patients with schizoid personalities have become psychotic on the average by the time they reach the middle twenties, that the psychosis has in one half of the cases persisted for over a year, and that one half of them had an insidious, indefinite onset. This statement, which agrees with the consensus on the subject, does not take into account the variability in the other half of the cases. Similar conclusions, however, appear frequently in psychiatric literature because certain significant observa-

tions which are true for only a limited number of cases are held to be true for the group as a whole.

*Diagnosis.*—Since the schizoid type of personality is considered a predisposing factor in schizophrenia, it was to be expected that most of the cases with the special constellation of traits outlined would fall into the schizophrenic group. These cases were selected regardless of diagnosis from a total group that included the diagnoses shown in table 3.

The diagnoses made at the Boston Psychopathic Hospital in the cases of the 33 patients with schizoid personalities are given in table 4, as well as the diag-

TABLE 3.—*Diagnoses in Group of 327 Cases*

Diagnosis	Number of Cases	Per Cent
Schizophrenia.....	151	46.2
Affective psychoses.....	79	24.2
Paranoid condition.....	12	3.7
Dementia paralytica.....	17	5.2
Schizo-affective psychoses *	28	8.5
Undiagnosed psychoses.....	23	7.0
Others.....	17	5.2
	327	100.0

\* By these we mean psychoses in which the clinical picture included both the schizoid and affective elements and the differential diagnosis could not be made. See the forthcoming paper by one of us (Kasanin) in the American Journal of Psychiatry entitled "The Acute Schizo-Affective Psychoses."

TABLE 4.—*Diagnoses in the Cases of Patients with Schizoid Personalities*

	Diagnosis at Boston Psycho-pathic Hospital		Diagnosis at State Hospital					At B. P. H. Only
	Number of Cases	Per Cent	Schizo-phrenia	Affective-Manic Condition	Affective-Depressed Condition	Affective Stupor	Paranoid Condition	
Schizophrenia.....	24	72.7	12	2*	..	1*	1*	8
Affective-manic condition.....	2	6.1	2*	..	..	..	..	..
Affective-depressed condition.....	1	3.0	..	..	1	..	..	..
Paranoid condition...	2	6.1	..	..	..	..	1	1
Schizo-affective psychoses.....	2	6.1	2*	..	..	..	..	..
Undiagnosed psychoses.....	1	3.0	1*	..	..	..	..	..
Psychasthenia.....	1	3.0	..	..	..	..	..	1
	33	100.0	17	2	1	1	2	10

\* The diagnosis made at the Boston Psychopathic Hospital was not confirmed at the state hospital.

noses made at the state hospital in the cases of the patients who went to state hospitals. Ten patients were discharged into the community and never entered another hospital.

It is seen that with the exception of 2 patients, 1 in whose case a diagnosis of an affective-depressed psychosis was corroborated at the state hospital and 1 psychasthenic patient who did not go to a state hospital, all the patients had been considered at one time or another as having schizophrenia (including paranoid condition). We have observed that when a person with a constellation of traits such as we have emphasized breaks down with an affective psychosis, an analysis of the clinical picture reveals that there are a great many features in it which

give the affective disorder a strong schizophrenic coloring. Thus, in the patient whose condition was diagnosed as a depression, there were vague ideas of reference, fear of death and insanity, impulsive and odd behavior and possible auditory hallucinations, which were elicited when this patient was studied for a longer period at a state hospital.

A final review of the 9 cases in which the diagnosis was changed in state hospitals was made by Dr. Karl M. Bowman, a research consultant at the Boston Psychopathic Hospital. He assigned 5 of the cases to the schizo-affective group (the classification used for cases showing both schizophrenic and affective components); 3 definitely to the schizophrenic group, and 1, with a marked schizophrenic reaction, to the undiagnosed psychoses, because of an organic element. The final realinement of these 33 cases shows: schizophrenia, 24; paranoid condition, 1; affective-depressed condition, 1; schizo-affective psychoses, 5; undiagnosed psychoses, 1, and psychasthenia, 1.

TABLE 5.—*Clinical Symptoms in Thirty-Three Cases*

Behavior	No. of Cases	Talk	No. of Cases
Normal.....	8	Normal.....	8
Underactive.....	14	Undertalkative.....	14
Overactive.....	7	Overtalkative.....	6
Stuporous.....	4	Mute.....	8
Odd or queer.....	14	Odd or queer.....	9
No constant pattern.....	8	No constant pattern.....	7

Mood	No. of Cases	Hallucinations	No. of Cases	Delusions	No. of Cases
Normal.....	1	None.....	12	None.....	3
Irritable.....	9	Voices.....	14	Persecutory.....	19
Apathetic.....	16	Other auditory.....	1	Misinterpretations.....	14
Depressed.....	15	Visual.....	3	Erotic.....	12
Inappropriate.....	11	Olfactory.....	3	Grandiose.....	8
Agitated.....	11	Somatic.....	2	Arehale.....	6
Afraid.....	9	Others.....	1	Religious.....	5
Elated.....	7	Unknown.....	6	Hypochondriac.....	5
Suspicious.....	4			Self-accusatory.....	5
Others.....	3			Others.....	4
No constant pattern.....	7			Unknown.....	1

It is therefore seen that 72.7 per cent of the patients with the constellation of traits which we have called the schizoid personality fall into the schizophrenic group, but that only 15.9 per cent of all persons with schizophrenia have this special type of personality.

*Clinical Symptoms.*—The symptoms on which the foregoing diagnoses were based may be summarized for the 33 cases under the headings used on the code sheet. Most of these cases were coded for more than one item (table 5).

*Rate of Recovery.*—All patients were followed as a routine measure for a period extending beyond that of their residence in the hospital. The patients who were discharged into the community were followed by social workers, while patients who were transferred to state hospitals were visited by research psychiatrists after six months. Of our patients, 10 went directly from the Boston Psychopathic Hospital into the community and 23 were either transferred directly to or later entered state hospitals. Those of our patients who were still in hospitals at the time our study was made were followed by letter in addition to the routine six-month follow-up. In this way, information on the 33 cases was had over a period ranging from less than six months following discharge from the Boston Psychopathic Hospital, in the case of one patient (who died), to a period of

three and one-half years in the case of another. The average length of time that these cases were under our observation was twenty months.

At the end of this period, 8 of our patients had recovered,<sup>3</sup> or 24.2 per cent. Improvement was shown in 6 others, or 18.4 per cent. It was known definitely that 19 other patients, or 57.5 per cent, had not recovered. Fifteen of these patients were still in state hospitals at the time of the last follow-up, 2 had died and 2 were being cared for at home.

It is of interest to compare our figures, small as they are, with recovery rates based on the total population in state hospitals. Figures have been taken from the United States Census Publication for 1923,<sup>4</sup> and from the Annual Report of the Massachusetts Commissioner of Mental Diseases for the year ending Nov. 30, 1929.<sup>5</sup> In both instances the figures are based on the total number of discharges. We are including percentages for all diagnoses and for schizophrenia, since most of our cases fall into this group (table 6).

It must be noted that our percentages are based on all cases, both discharged and in hospital, whereas all the other figures were computed on the basis of discharges only. General recovery rates per hundred admissions are given as

TABLE 6.—Comparison of Recovery Rates

	Recovered, per Cent	Improved, per Cent
Schizoid personalities .....	24.2	18.4
All United States hospitals—all diagnoses.....	23.3	46.2
All Massachusetts state hospitals—all diagnoses.....	21.2	59.7
All United States hospitals—dementia praecox.....	11.2	58.5
All Massachusetts state hospitals—dementia praecox.....	8.3	70.3

13.6 for all diagnoses, and 6.4 for schizophrenia in the United States Bureau of Census Publication, for which we have no comparable figures.

It is of some significance that our cases in which the patients showed a definitely malignant personality and in which the onsets were very insidious, cases which usually carry with them the worst prognosis, had a recovery rate higher than that for all diagnoses (in the figures quoted) and very much higher than that for schizophrenia. We can correlate outcome in these cases with diagnosis, onset and duration of the psychosis.

*Recovery and Diagnosis.*—Of the 8 recovered patients, 7 had been considered to have schizophrenia at the Boston Psychopathic Hospital and 1 had been called psychasthenic. Three of the patients whose disorder had been called schizophrenia had been transferred to state hospitals before recovery, where the diagnosis was corroborated in 1 case, changed to paranoid condition in 1, and to manic-depressive stupor in the other.

3. The criteria on which these terms are based are the same as those used in the report of the Bureau of Census. "Recovered" means that the patient has regained his normal mental health so that he has practically the same status as before his illness; "improved" means any degree of mental gain less than that of recovery; "unimproved" means that he has made no mental gain.

4. Patients in Hospitals for Mental Disease, U. S. Bureau of the Census, 1923.

5. Annual Report of the Massachusetts Commissioner of Mental Diseases, 1929.

*Recovery and Onset.*—The type of onset has been associated with outcome as shown in table 7. It is seen that of the 15 patients whose psychotic condition had had an insidious, indefinite onset, 10, or 66.6 per cent did not recover; in 50 per cent of those who recovered the condition had had an acute, definite onset. Neither of these observations is statistically significant.

TABLE 7.—Correlation of Onset and Outcome

Onset	Outcome			Total
	Recovered	Improved	Not Recovered	
Acute definite.....	4	2	1	7
Subacute definite.....	1	0	3	4
Insidious definite.....	1	0	3	4
Subacute indefinite.....	0	1	0	1
Insidious indefinite.....	2	3	10	15
Unknown.....	0	0	2	2
	8	6	19	33

TABLE 8.—Correlation of Duration of Psychosis Previous to Admission with Outcome

Duration of Attack	Outcome			Total
	Recovered	Improved	Not Recovered	
7 to 31 days.....	3	2	0	5
1 to 6 months.....	3	0	2	5
7 to 11 months.....	1	0	5	6
Over 1 year.....	0	2	3	5
Over 2 years.....	1	2	7	10
Unknown.....	0	0	2	2
	8	6	19	33

TABLE 9.—Correlation of Duration of Psychosis up to Time of Last Follow-up with Outcome

Duration	Outcome			Total
	Recovered	Improved	Not Recovered	
7 to 31 days.....	1	0	0	1
1 to 6 months.....	3	0	1	4
7 to 11 months.....	2	1	0	3
Over 1 year.....	1	1	3	5
Over 2 years.....	1	2	6	9
Over 3 years.....	0	2	1	3
Over 4 years.....	0	0	8	8
	8	6	19	33

*Recovery and Duration of Psychosis Previous to Admission.*—The duration of the psychosis previous to admission, as given on the code sheet by clinical estimate is correlated with outcome in these cases as shown in table 8.

*Recovery and Duration of Psychosis up to Time of Last Follow-Up.*—Both tables 8 and 9 indicate, in these cases, that the longer the duration of the psychosis the less is the chance of recovery; whereas some of these patients with schizoid personalities did have an acute and brief psychotic episode with recovery.

*Clinical Picture.*—We are unable to find any similarities in clinical pictures. A very superficial review of our material allows certain generalizations, but more thorough study of the cases, especially of the clinical pictures, shows a definite variation from case to case, which can best be illustrated by a report of several.

#### REPORT OF CASES

CASE 1.—A woman, aged 47, had always been essentially energetic, critical and prudish, but at the same time extremely irritable and suspicious; she had been a difficult person to get along with, and had had to be "handled with kid gloves" by her employers as she was always looking for trouble. Although possessing all the traits enumerated in our constellation, she was at the same time self-willed, temperamental, excitable and quite interested in the external world. Her psychosis was an exaggeration of her suspiciousness, and was marked by many misinterpretations and a feeling that she was wanted sexually by her employer and other men. The clinical picture consisted of feelings of hostility and persecution, marked irritability and occasional aggressiveness. With this there was, however, excellent contact with the outside world, accessibility, and fair cooperation in treatment. Her condition has remained unchanged for two and a half years.

CASE 2.—The patient was a shy, timid, "mouse type" of woman, aged 33, who was extremely sensitive, introverted and seclusive, a person who always kept in the background. She was a conscientious worker in a large corporation, where "she took dictation without ever raising her eyes from her book." Here she came in contact with a liberal and perhaps even radical employer, who expressed modern ideas about marriage and sex. During her association with this man she gradually began to feel that there was some magical influence exercised by him on her and that she was being in some way seduced, although as a fact he had never even spoken directly to her. She came to the Psychopathic Hospital depressed and apprehensive, and spoke freely about her ideas, about the voices she heard and about various sensory experiences such as a light projected on her genitals by her employer so that she might have sexual feelings. During all this she was accessible and cooperative, and spoke freely about her difficulties; after a very brief review of her problems, she entirely recovered from the illness, which lasted almost two years.

CASE 3.—The patient, a temperamental, imaginative American-born Italian girl, aged 18, had spent her childhood in Italy after the death of her father. When she returned to America she became engaged in a somewhat unorthodox fashion. While waiting for a more formal proposal to be made to her family, the casual visit of a strange man threw the patient into a terrific panic; this was followed by a delirium in which she had hallucinations and expressed a number of odd ideas. In the hospital she was in a state of fear; she screamed, sobbed, cried and cooperated very poorly. She would not allow anybody to examine her physically, expressed ideas of unworthiness and guilt, thought that the food was poisoned, and heard voices. This lasted only a short time, after which she was able to go home and adjust herself to her family. She is now said to be a "different girl," sociable, cheerful and "peppy."

CASE 4.—A girl, aged 20, had been a shy, sensitive child, extremely touchy about the fact that she was a Jew and so seclusive in school that nobody could remember her. Quite suddenly, at the age of 17, she became overtalkative, cried a good deal, and slept most of the time; she recovered six months later. On

returning to school she did brilliant academic work and graduated with honors. She was admitted to the Psychopathic Hospital two years later when she became extremely seclusive and depressed and cried a good deal. She entered the hospital in a state of stupor. After a year and a half of extreme stupor she showed signs of complete disorganization of personality, with periods of excitement, violence and regression. She is still in the hospital.

*Comment.*—The clinical pictures in these four cases of women showed little in common. In the cases of the men the situation is essentially the same.

CASE 5.—A tall, handsome boy, aged 22, somewhat effeminate, at the age of 15 had had a breakdown which kept him out of school for three months. At the age of 22, the patient became depressed, cried a good deal and had ideas that he was the Noble hammer murderer and that his girl had been murdered. He became clear for a week, then again became tearful, cried and laughed at the same time, talked incoherently, and became so difficult to handle that he was brought to the Psychopathic Hospital. In the hospital his behavior was bizarre; he sang hymns, spoke a great deal about sex perversions, and tried to get to the center of the roof, explaining that he was trying to reach his father. He wanted to die, and baptized himself with coffee and urine. He said that detectives were after him, spoke of persecutions, and felt that his father was near him. There was also an open homosexual conflict, with confession of guilt. After a few months at a state hospital the patient recovered and was able to return to his family.

CASE 6.—A boy, aged 19, had been always an "odd stick" in his own family and not able to mix with his brothers or schoolmates. There was gradual slumping in efficiency, with more and more withdrawal, until finally he expressed ideas that the neighbors set dogs to bark at him and that people laughed at him on the street. At the Psychopathic Hospital he was extremely passive, withdrawn and unproductive, but occasionally asked for medical treatment. He was taken home, where he became more and more withdrawn and finally had to be committed to a state hospital. This case may be compared with case 4, the girl who was also a nobody in school, but in whom there were marked fluctuations in mood, which this patient never exhibited.

CASE 7.—A sensitive, intelligent lad, aged 22, by tremendous effort was able to become a leader in a small country high school as a compensation for shyness and a feeling of inferiority which were fostered a great deal by parental rejection. On coming to Boston the patient became more and more seclusive, could not be made to mix with other people, and would bolt from the parlor of the boarding house whenever there was a gathering there. He finally expressed ideas that people were talking about him and laughing at him, that he was the center of interest for the whole world, and that his actions and behavior were being broadcast. This shy and harmless boy felt that he was accused of being a sadist and that his remarks appeared in the newspapers and over the radio. All this was expressed in a setting of a good deal of tension, apprehension and some depression, the whole clinical picture changing for the better within a few months, with a complete return of industrial and social efficiency.

CASE 8.—A boy, aged 17, a keen, alert youngster, much interested in school and in dramatics, for over a year had brooded about insanity in his family and began to fear that he would go insane. While on a visit to the country home of

a social worker, who had become interested in him, he developed the fantasy of a sexual relationship with her in a setting of panic. On returning to school in the fall the patient brooded more and more, and quite suddenly accused his history teacher of talking about him during a lecture on the American constitution. The patient was reassured by his teacher, but a few days later was found dazed on the street and brought to the hospital. Here he was restless, tense and anxious, but quite talkative. He spoke about being hypnotized, said that members of the family were killed, that people talked about him, and that he might have been a radio or a broadcasting station. He gave evidence of auditory hallucinations without clearly revealing their content. In the state hospital the patient continued to be extremely perplexed and afraid, and beset by hallucinations. He had alternating periods of socially acceptable conduct, when he was allowed to go home on a visit, with subsequent return to the hospital where he is at the present time.

*Comment.*—A review of the formulations made for each case on the basis of fairly obvious material in the case histories revealed no consistency. Summaries of each case had been prepared containing the essentials of the clinical picture, the formulation of the case and the reconstruction of the fundamental mechanism. Even in cases in which the mechanisms were considered the same, such as a wish-fulfilling fantasy or a projection of a feeling of guilt on the outside world, the clinical pictures still showed wide variability. In comparing patients with antithetical personality traits, such as aggressive and passive behavior trends, we found that in both types some patients had hallucinations, ideas of reference or an erotic component, while others did not. Furthermore, it could not be demonstrated that the clinical picture of patients who recovered differed from that of patients who did not recover. We had felt that patients with a fairly good social adjustment before the psychosis and with favorable environmental opportunities might have a better outcome, but could not corroborate this hypothesis from our cases. In both groups there were fantastic ideas, odd behavior, regression and crude sexual archaic manifestations. Perhaps if the fundamental dynamics in each case had been studied and compared, some principle underlying all these reactions might have been manifest. As yet, however, we can only speculate as to what are the dynamic forces in schizophrenia and the other functional psychoses.

One reason for the dissimilarity in the clinical picture is probably the fundamental variation among persons due to a difference in constitutional endowment, environmental influences and life experiences. The attempt to generalize about clinical pictures and to find certain uniformities of sequence is difficult if there is any psychologic analysis of the individual and his environment. It was only the genius of Kraepelin which was able to see the material en masse and to make certain crude generalizations.

## PERSONALITY

Since the personality of the patient may account for some of the variations in the clinical picture, we must turn to a consideration of this factor. We know that in 19 of these cases the prepsychotic personality was thought to be of definite etiologic significance in the final breakdown and was questioned in 6 others. In 11 of the cases the personality had been considered "different" from early childhood, and in 14 cases the psychosis was thought to be the evolution of a special type of personality. Since the constellation of traits which we have outlined

TABLE 10.—*Personality Traits Occurring Most Frequently*

In 151 Cases of Schizophrenia			
Childhood	Per Cent	Adult	Per Cent
1. Neurotic traits.....	68.9	1. Total abstainers.....	66.8
2. Extremely sensitive *.....	52.3	2. Close-mouthed *.....	65.6
3. Shy, followers *.....	43.0	3. Nonsmokers.....	61.5
4. Close to family.....	38.4	4. Extremely sensitive *.....	56.8
5. Few friends *.....	35.8	5. Few friends *.....	53.6
6. Unusual attachments.....	29.8	6. Shy, followers *.....	51.2
7. Little self-assertiveness.....	27.1	7. Neurotic traits.....	50.4
8. Model child.....	26.4	8. Solitary amusements *.....	43.2
9. Solitary amusements *.....	25.2	9. Great ambition.....	43.1
10. Frequent day-dreaming.....	23.8	10. Close to family.....	39.2
In Total Number of 327 Research Cases			
1. Neurotic traits.....	61.6	1. Total abstainers.....	63.5
2. Extremely sensitive *.....	49.5	2. Nonsmokers.....	61.1
3. Close to family.....	45.9	3. Close-mouthed *.....	52.2
4. Shy, followers *.....	33.1	4. Extremely sensitive *.....	52.1
5. Unusual attachments.....	29.1	5. Neurotic traits.....	50.0
6. Few friends *.....	28.8	6. Valuable workers.....	47.2
7. Model child.....	25.7	7. Close to family.....	44.6
8. Recreation with others.....	25.4	8. Great ambition.....	43.2
9. Great output of energy.....	25.0	9. Few friends *.....	39.4
10. Little self-assertiveness.....	23.5	10. Very sympathetic.....	39.4
11. Solitary amusements *.....	22.9	11. Shy, followers *.....	33.1
12. Keen sense of humor.....	21.7	12. Solitary amusements *.....	29.9

\* Traits found as often or more often than the five cardinal schizoid traits selected by the authors.

does not fully describe the personality as a whole, a consideration of the other personality traits which were coded in these cases may throw some light on what characteristics tend to be associated with the five traits which we have assumed to be the core of the schizoid personality. In this way we shall attempt to answer the question as to whether these traits adequately and validly constitute the intuitive clinical concept of the schizoid personality.

*Frequency of Cardinal Schizoid Traits.*—It may first be of interest to note the individual frequencies of the five cardinal schizoid traits in the entire group of 327 patients and in the 151 patients with schizophrenia, from among whom were chosen patients showing all five traits. With the exception of close-mouthedness, these traits were coded both for childhood and adult personality. Attention must be given to the fact that actually the five traits which we arbitrarily selected to

define the schizoid personality are not those appearing most frequently either among the schizophrenic patients or in the total number of patients studied in the research. For this reason, we have listed the other traits that were found as often as or more often than those we selected.

We wish again to refer to the fact that only 33 of the total number of 327 patients (10.1 per cent) and 24 of the 151 patients with schizophrenia (15.9 per cent) had the constellation of all five traits which we used as the criteria of the schizoid personality.

*Associated Personality Traits.*— In order to determine what traits are significantly associated with the cardinal five traits, we have used as a control all other patients studied in the research not possessing this complex of traits. Of this sort there were 294. A table has been prepared for the comparison of traits coded in our group with those coded in the controls. Only those traits are considered which were present in either the schizoid or the cycloid extreme. As has been said before, those traits were designated as schizoid which are commonly held to be associated with schizophrenia, and their opposites, which are described in the prepsychotic phase of affective disorders, are referred to as cycloid. The cycloid extreme of each trait has been numbered in the table to agree with the schizoid.

Comparison has been made of percentages computed on the basis of the number of patients in whom the trait occurred as against the total number, 33 for the group with schizoid personalities and 294 for the controls. Wherever a trait has been coded for both childhood and adult life the total number of persons in adult life was less than the entire number, namely, 29 and 255, because 4 patients in our schizoid group and 39 in the control group became psychotic in childhood (before 16) and were therefore not coded for adults. However, when provision was made for coding traits only in adult life all patients were included, since patients who broke down in childhood were coded for adult traits on the basis of childhood personality.

In table 11, percentages are given for both the schizoid and the control cases, and the differences are indicated. The standard deviation of the difference between the two percentages has been calculated for each trait according to the formula:

$$\text{S.D. of } p_1 - p_2 = \sqrt{\frac{p_1(100-p_1)}{n_1} + \frac{p_2(100-p_2)}{n_2}}$$

$p_1$  and  $p_2$  are the percentages given in each trait for the schizoid personalities and control cases, respectively, and  $n_1$  and  $n_2$  are the total number of cases in each group respectively.

From table 11 it is seen that, on the whole, schizoid traits run higher in the group with schizoid personalities as indicated by plus

differences, and that cycloid traits run higher in the controls as indicated by minus differences. Four exceptions are of interest. We have assumed that in respect to "relationship to family," the schizoid extreme would be a close relationship, since the schizoid person is notably dependent on his family and closer to them because of his avoidance of outside social contacts; whereas the cycloid trait would be distant from the

TABLE 11.—*Personality Traits in 33 Cases with Schizoid Personalities as Contrasted with 294 Control Cases*

Schizoid Traits	Childhood			Adult		
	Per Cent Schizoid Personalities	Per Cent Control Cases	Difference	Per Cent Schizoid Personalities	Per Cent Control Cases	Difference
1. Only child.....	9.1	10.9	— 1.8			
2. Model child.....	30.3	25.2	+ 5.1			
3. Neurotic traits.....	81.8	62.6	+19.2*	65.5	48.2	+17.3
4. Close to family.....	42.4	46.2	— 3.8	48.3	44.3	+ 4.0
5. Unusual attachments.....	39.4	27.9	+11.5	48.3	26.6	+21.7*
6. Unusual resentments.....	15.2	9.5	+ 5.7	24.1	9.8	+14.3
7. Feeling of inferiority.....	.....	.....	.....	54.5	21.4	+33.1†
8. Inferiority and superiority.....	.....	.....	.....	12.2	2.4	+ 9.8
9. Very sympathetic.....	.....	.....	.....	21.2	8.8	+12.4
10. Fusses over pain.....	.....	.....	.....	36.4	17.3	+19.1*
11. Little self-assertiveness.....	54.5	20.1	+34.4†	58.6	20.4	+38.2†
12. Teased by associates.....	21.2	12.6	+ 8.6	17.2	10.6	+ 6.6
13. No sense of humor.....	27.2	9.8	+17.4*	37.9	9.8	+28.1†
14. Extremely jealous.....	9.1	7.8	+ 1.3	13.8	11.4	+ 2.4
15. Poor sportsmanship.....	21.2	10.5	+10.7	31.0	13.7	+17.3
16. Frequent day-dreaming.....	36.4	17.7	+18.7*	65.5	23.1	+42.4†
17. Very absent-minded.....	.....	.....	.....	33.3	10.9	+22.4†
18. Little output of energy.....	36.4	8.1	+28.3†	48.3	7.8	+40.5†
19. Variable output of energy.....	3.0	5.8	— 2.8	0.0	11.7	—11.7†
20. Little initiative.....	.....	.....	.....	30.3	15.6	+14.7
21. Little ambition.....	.....	.....	.....	18.2	12.9	+ 5.3
22. Inferior workers.....	.....	.....	.....	6.0	4.1	+ 1.9
23. Regular church-goers.....	.....	.....	.....	45.4	25.2	+20.2*
24. Nonsmokers.....	.....	.....	.....	84.8	58.6	+26.2†
25. Total abstainers.....	.....	.....	.....	78.8	61.8	+17.0*
Cycloid Traits						
2. Delinquent child.....	0.0	2.4	— 2.4†			
4. Distant to family.....	24.2	8.8	+15.4*	24.1	14.1	+10.0
7. Feeling of superiority.....	.....	.....	.....	12.2	22.1	— 9.9
9. Very sympathetic.....	.....	.....	.....	18.2	30.6	—12.4
11. Extreme self-assertiveness.....	15.2	16.7	— 1.5	17.2	22.7	— 5.5
13. Keen sense of humor.....	0.0	24.1	—24.1†	0.0	31.4	—31.4†
18. Great output of energy.....	15.2	26.2	—11.0	6.9	30.6	—23.7†
20. Great initiative.....	.....	.....	.....	6.0	21.7	—15.7†
21. Great ambition.....	.....	.....	.....	36.4	43.8	— 7.4
22. Valuable workers.....	.....	.....	.....	39.4	47.9	— 8.5
23. Irregular church-goers.....	.....	.....	.....	15.1	22.8	— 7.7
24. Heavy smokers.....	.....	.....	.....	0.0	11.6	—11.6†
25. Heavy drinkers.....	.....	.....	.....	0.0	6.8	— 6.8†

\* The difference is more than two times the standard deviation and is considered statistically significant.

† The difference is highly significant.

family, since the cycloid type has no difficulty in making friends outside of the smaller family group. Actually, however, our patients are less outstanding in their close attachment to the family during childhood than the controls, although the difference is small in both childhood and adult life; but there are more patients distant to the family in our group than in the other, significantly so in childhood.

The other traits which we had assumed to be schizoid traits, "only child" and "variable output of energy," occurred a little more frequently

in the control group and significantly so in adult life for the latter. It is to be noted that two cycloid traits, "great ambition" and "valuable workers," occur in about a third of our cases.

By a simple statistical test, the calculation of the standard deviation of the difference, we have been able to determine what traits tend to accrue to our original constellation of five traits. In table 11, such traits are indicated by plus differences with the addition of an asterisk.

"Little self-assertiveness," "no sense of humor," "frequent day-dreaming" and "little output of energy" occur both in childhood and in adult life, although more frequently in adult life. Of traits coded in adult life only, "feeling of inferiority," "fusses over pain," "very absent-minded," "regular church-goers," "nonsmokers" and "total abstainers" have a significant incidence among the schizoid personalities. In childhood, "neurotic traits" appear more frequently to a significant degree among the schizoid personalities, although they show a definite decrease in adult life; while "unusual attachments" to a member of the family

TABLE 12.—Percentage of Total Number of Codings for All Traits

	Childhood				Adult			
	Schizoid	Cycloid	Average	Unknown	Schizoid	Cycloid	Average	Unknown
Schizoid personalities	47.0	3.6	39.2	10.2	55.3	7.6	31.1	5.9
Controls....	25.4	9.4	55.9	9.3	26.7	16.4	51.2	5.7

and "variable output of energy are significant in adult life only. Several cycloid traits have a definite negative, association with our trait-complex (as indicated by minus differences), namely, "delinquent child," "keen sense of humor," "great output of energy," "great initiative," "heavy smokers" and heavy drinkers."

The inference may be drawn that on the whole those cases which have the particular constellation of traits which we have designated as the core of the schizoid personality tend to have associated with them, more significantly than in the control cases, other schizoid traits of which those cited are the most striking.

This conclusion is borne out by comparing percentages of the total number of codings for all traits in the schizoid, cycloid, average and unknown categories, for both the 33 schizoid patients and the 294 controls (table 12).

From both the composite table and the tables giving individual traits it can be seen that generally there is an increase in the percentage of schizoid traits in adult life in the schizoid group. This may mean that such persons do actually become more schizoid as they grow older, but it must be remembered that in adult life there are 33 cases in which the constellation of personality traits outlined is exhibited, while

in childhood there are only 16. Hence it would seem that the more often the complex of schizoid traits selected by us occurs, the more often will other schizoid traits appear. In three instances only, "neurotic traits," "teased by associates" and "variable output of energy," there is a falling off in adult life.

By utilizing the code sheets, a constellation of traits may thus be assembled empirically, the validity of which must next be questioned. It was hoped that an analysis of the more integrated description of the personality, given in the medical and social histories, might likewise give some clearcut delineation of the schizoid type.

*Other Personality Traits.*—It was striking that certain descriptive terms were used in reference to the personality of these patients other than those included in the personality outline. Such traits have been

TABLE 13.—Other Traits Describing Schizoid Personalities

	Per Cent		Per Cent
1. Stubborn.....	45.5	20. Feels "different".....	18.1
2. Imaginative.....	45.5	21. Broods.....	15.2
3. Unstable, moody.....	42.4	22. Craves attention.....	15.2
4. Timid, cowardly.....	42.4	23. Irresponsible.....	15.2
5. Quiet.....	39.4	24. Quarrelsome.....	15.2
6. Irritable.....	36.4	25. Immature.....	15.2
7. Suspicious.....	36.4	26. Pities self.....	12.2
8. Conscientious.....	30.2	27. Critical, sarcastic.....	12.2
9. Easily teased.....	30.2	28. Selfish.....	12.2
10. Serious.....	27.2	29. Avoids difficulties.....	12.2
11. Hurt by criticism.....	27.2	30. Hard to manage.....	12.2
12. Depressed, gloomy.....	27.2	31. Unpractical.....	11.0
13. Well liked.....	24.2	32. Frugal, saving.....	11.0
14. Worrisome.....	24.2	33. Unclean.....	11.0
15. Dependent.....	21.2	34. Domineering.....	6.0
16. Studious.....	21.2	35. Prudish.....	6.0
17. Insecure.....	21.2	36. Happy.....	6.0
18. Docile.....	21.2	37. Indifferent to opinion.....	6.0
19. Retiring.....	21.2		

listed in the order of their frequency whenever they occurred in more than one case. It must be remembered that these traits were not investigated as a routine as were those on the personality outline, and were noted in the case record only when they were so outstanding as to be used spontaneously by the informant, or were suggested to the informant by the individual physician or social worker taking the history. Such terms as quiet, retiring, timid fall into the first group, whereas such terms as stubborn, suspicious, imaginative tend to be part of the average psychiatrist's vocabulary. These traits are listed, however, for what they may be worth (table 13). All that can be said about these traits is that they are suggestive for future investigations. It will be observed that many of them occurred as frequently as, or more often than, the traits in the outline.

*Variability of Cardinal Traits.*—A consideration of these patients in terms not of traits but a total personality configuration revealed a startling variability in general make-up. It was striking that so little

homogeneity existed in a group sharing a common constellation of traits. In fact, even when associated characteristics in their innumerable combinations were disregarded, there still remained a great variation in the manifestation of traits in which these patients presumably resembled one another.

**Seclusiveness:** It must be remembered that the adjectives by which we have described these patients, such as seclusive, sensitive and uncommunicative, are extremely general. We are aware of the fact that seclusiveness, for instance, is a complex psychopathologic and social phenomenon, which may come from a large number of causes and may be quite varied in its expression. These seclusive patients seemed to fall into several categories, according to the mechanism of seclusiveness.

In group 1 we found patients who were passive and withdrawn, with no interest in the outside environment, who could not be budged from their passivity even in the best days of their mental health. Typical of this group is case 4, in which the patient remained so distant from her schoolmates and shared so little in their interests or games that neither her teachers nor her classmates could remember that such a person existed.

In group 2 we found a kind of seclusiveness which was a function of the environment. Here were patients who were very shy and who could never make the first step, but who, on being prodded along, would become fairly good mixers and intimately associated with the interests of a larger environment. One such patient was a brilliant, proud, superior British girl, who felt herself unwelcome when among high school flappers of her own age shortly after emigrating to America. The same girl blossomed out into a friendly and sociable person when she assumed a position of responsibility in which other girls appreciated and encouraged her special qualities.

In group 3 there were patients who had become defensively shut-in and seclusive on the basis of rejection by the social group, occasioned in the first place by their unacceptable social manner. These patients were aggressive, vehement, suspicious, sour and intolerant. They had the unhappy faculty of making enemies rather than friends. In order to make life more bearable and to avoid arousing more hostility, they chose to be alone rather than to go on making enemies in the group. Their seclusiveness was their only shield against the outcropping of frank hostility toward themselves.

Group 4 illustrates the mechanism of superiority feeling, which is too familiar to need explanation in detail. It is obvious, however, that persons with a strong feeling of superiority naturally shun the majority of their fellow men, as for instance the proud, haughty Italian girl who received most of her education in Europe and who, on coming

to America, flatly refused to descend to the level of her inferior compatriots.

In group 5 the feeling of inferiority was operative in a large number of cases and varied from feelings of physical inferiority to those of social and economic inadequacy. In such cases the patients actively avoided social contacts and chose to be seclusive. We have called this a self-imposed seclusiveness. One patient, for example, was conscious of her inability to make a social adjustment among people whom she recognized to be her intellectual inferiors and for that reason refused to mix with them in the slightest degree. Another patient sneaked away from parties in his rooming house, to which he was always invited, because of self-consciousness induced by his inability to compete with other bright boys in the bank where he worked, although previously he had been the basket-ball hero in the small village where he was brought up.

It can be seen that unless these traits are completely analyzed in themselves, it is difficult to tie them up with later psychotic developments. Such an analysis as ours must be considered superficial even from a purely statistical point of view, because it only uncovers more and more variables, each of which must be properly evaluated, analyzed and further dissected. In this respect, of course, psychoanalysis has a definite scientific contribution as it has pointed out clearly the richness and variability of the psychic life of even the most ordinary person.

**Sensitivity:** What has been said about seclusiveness can be equally well applied to the other four traits. The feeling of sensitivity, for example, takes many different forms in these cases. It may relate to a special topic, such as a physical handicap, or may be a diffuse feeling of personal inadequacy. In many of these cases, sensitivity which may have been engendered by some special topic becomes irradiated throughout the total personality of the subject, whereas in the average person there may be a sensitiveness to one or more topics with a neutral reaction to all others. In other persons of this group there is a marked sensitivity to criticism, which seems to be based on a general feeling of inferiority or inadequacy, so that these patients find no resources in themselves on which they can fall back. In still others, the sensitivity is due to the fact that these persons relate everything in the environment to themselves. The important thing in the study of sensitivity is the determination of sensitizing agents, or in other words, of what the patient is sensitive about. It is necessary to go into the entire history of these persons to discover conditioning factors.

#### FACTORS CONDITIONING SCHIZOID TRAITS

**Heredity.**—A history of positive heredity was found in 28 (84.5 per cent) of these cases, among parents, siblings, collaterals and ancestors,

including psychoses with state hospital diagnoses and history of excessive alcoholism, feeble-mindedness, epilepsy, organic nervous disease, nervous breakdowns and outstandingly psychopathic trends. All statements as to heredity were weighed carefully before coding.

In 7 of the 28 cases in which a positive heredity was found, the mother was listed as psychotic in 4 cases in which definite diagnosis had been made at state hospitals, as questionably feeble-minded in 2 instances, and as of a depressive make-up 1. In 16 cases the father was coded as excessively alcoholic in 8, as unstable or psychopathic in 5, with a question of epilepsy in 1, of dementia paralytica in 1 and as frequently depressed in 1. In 8 cases positive heredity in the

TABLE 14.—*Factors in Parental Inadequacy*

	Mother	Father	Both	Total
Alcoholism.....	..	7	1	8
Mental disease.....	4	..	..	4
Desertion.....	..	6	..	6
Divorce.....	..	2	..	2
Separation.....	..	3	..	3
Constant quarreling.....	..	..	19	19
Neglect, indifference.....	2	13	..	15
Overprotection (fostering dependence).....	12	5	3	20

TABLE 15.—*One-Parent Families*

	Mother	Father	Total
Death.....	1	7	8
Desertion.....	..	6	6
Divorce.....	..	2	2
Mental disease.....	1	..	1
Working away from home.....	..	1	1
	2	16	18

siblings included psychoses in 2, excessive alcoholism in 3, epilepsy in 1, hysteria in 1 and a depressive make-up in 1. In 5 cases there was a history of mental disorder in ancestors of collaterals; in 2 cases only was there a definitely negative history, and in 3 cases the heredity was unknown.

We know definitely that in 3 cases the patient worried about mental disease in the family. It is, of course, practically impossible to distinguish between the effect of mental instability inherited from the parent and its direct environmental influence on the child.

*Family Situation.*—It is therefore of interest to consider the early home and parental influences that enter into the lives of these patients. First, in all cases, with the exception of 1 in which information was lacking, it was thought that the parents had been unsatisfactory in their rôle. This interpretation is based on evidence which can be classified under several headings. More than one factor has been

included for many of these cases in table 15. In the cases of desertion, divorce and separation, the patient remained with the mother in each instance. It is to be noted that in 20 of the cases the patient was overprotected, which would lead us to suspect that overprotection is a function of the weak child who requires special attention because of a defect either of personality or physical build, or of both.

In 18 of the cases, or 54.5 per cent, the absence of one parent resulted in what we have called a "one-parent family." The reasons listed in table 16 were given as causes.

In 3 cases the patient was away from both parents, having been taken to live with relatives owing to a psychosis of the mother in each instance. Altogether then, in 5 cases the mother was missing from the home and in 19 cases the father.

Since these cases have not been compared with a normal population, it cannot be said that the factors appearing here are of definite etiologic significance in the development of the schizoid personality. It is striking that the father has been notably inadequate in 21 of the cases (in which 11 patients were males and 10 females) for one or more of the reasons listed, and is known to have been a devoted parent and a stable person in 9 cases only. One could speculate as to the relationship between the absence of a satisfactory male ideal and the lack of masculine aggressive qualities in the schizoid group. The fact that the mother has of necessity had to assume the rôle of father, together with a certain amount of aggressiveness in many of these cases, may lead to a consequent submissiveness on the part of the child; it may also result in a certain amount of idealization of the mother and over-attachment to her, thus making the final emancipation of the patient as well as his psychosexual development delayed or impossible.

In 30 cases there was some indication that the patient's attitude toward his family was unhealthy. In the remaining 3 cases the patient's attitude could not be considered of importance since in 1 case no information was obtained pertaining to the family situation, and in the other 2 cases no information was given to show how the patient reacted to a home which was described as an undesirable one. Sixteen patients had definite feelings of resentment against a parent, in 11 instances against the father and 5 against the mother. In 22 cases there was a marked overattachment of preference shown to one parent—to the mother in 16 and to the father in 6. A preference for or fixation on the mother coexisted with a resentment toward the father in 7 of these cases, while in 3 of the cases the resentment was against the mother and the attachment to the father. In 2 of the cases the patient was overattached to both parents. One other patient was abnormally devoted to a sister while resenting an older brother. In 4

cases the patient held himself aloof and distant from the family as a whole.

In 5 cases there was evidence to show a resulting feeling of insecurity, described as "feels left out, unwanted, misunderstood." In 5 other cases, the patient was sensitized by the home situation and was said to be "ashamed of home, Jewish customs, family situation, family brawling." In 3 other cases dissatisfaction was felt with the home because the patient "did not like the neighborhood, was not suited by the home, resented the lack of physical comforts." The patient worried over heredity in the family in 3 cases. Economic difficulties were a source of worry in 4 others. In all there was economic instability in 20 of the homes and frequent moving, which necessitated change in schools and companions, in 7 cases.

It can be concluded that in these cases the family situation and home life fostered feelings of resentment, insecurity, sensitivity or dependence in these patients. We can only speculate as to whether the traits we are studying developed in relation to such external influences or were original tendencies aggravated by unfortunate circumstances.

*Physical Factors.*—By far the greatest factors in determining sensitivity in these patients, however, were physical defects and anomalies. The medical histories of these patients proved to be of great interest. On admission to the hospital, a routine physical examination revealed that in 25 cases there were physical abnormalities which included neurologic disorders, fever and definite and indefinite physical diseases. In only 6 cases were endocrine disturbances found; in 5 cases, dystrichosis, and in 10 cases, vasomotor disturbances. Laboratory findings were negative except for 7 cases in which urinalysis showed some abnormalities, and 23 cases in which the white blood count was over 10,000.

In 21 cases a physical complaint, actual or fancied, had preceded hospital admission. In 3 cases only was there no history of physical defect or anomalies of long standing; one of these patients came into the hospital with a fever of unknown origin which suggested a definite toxic factor in the psychosis.

In the remaining 30 cases, however, the physical findings were such as might well have had some effect on the development of a particular type of personality, as well as a rôle in the etiology of the psychosis. This effect was specified plainly in 24 of the cases; in 10 of these cases the patient was extremely sensitive about a physical inferiority; in 10 others the physical defect was of such nature as actually to interfere with the patient's life adjustment, while in 4 cases the patient was both sensitive about and handicapped by a physical ailment.

TABLE 16.—Physical Factors (Males)

Case	Physical Factor				Reaction of Patient		
	Constitutional Anomaly	Diagnosed Physical Disease	Undiagnosed Physical Disease	Not Coded	Sensitive	Handicapped	Others
1	.....	.....	Disorder of coordination upper extremities following injury to head at 1	Sickly child; nervous stomach, nausea	.....	Schooling interrupted; avoids physical exercise; exaggerates physical ailments	.....
2	.....	Deaf on one side following mastoidectomy at 9 months	.....	Injury to head at 8	Deafness, height (6 feet, 2 inches)	.....	.....
3	.....	.....	.....	Underweight	.....	.....	Not specified
4	Tall, awkward	.....	.....	.....	Size (6 feet, 2 inches)	.....	.....
5	Retarded development; pigeon breast	.....	.....	Sickly baby; premature birth at 7 months	.....	No interest in physical exercise; easily tired	.....
6	Inferior physique	.....	? skull fracture at birth	.....	.....	.....	Exaggerated physical ability
7	.....	.....	.....	"Feminine habitus"; nasal obstruction	.....	.....	Not specified
8	.....	.....	Injury to head at 5	Nasal obstruction	.....	Preoccupied with nose	.....
9	.....	.....	.....	.....	Bowlegs, acne, small stature	.....	.....
10	Physical frailty all through childhood	.....	.....	Convulsions; bilious attacks in childhood	Weakness	Too frail to play	.....
11	.....	.....	.....	Underweight; deviated septum; injury to head at 13	.....	Preoccupied with health	.....
12	Poor physique; underweight	.....	.....	.....	.....	Picked on because "skinny and small"	.....
13	Physical inferiority; poor development; pigeon breast	.....	? old rachitis; underweight	.....	.....	.....	Not specified

TABLE 17.—Physical Factors (Females)

Case	Physical Factor				Reaction of Patient		
	Constitutional Anomaly	Diagnosed Physical Disease	Undiagnosed Physical Disease	Not Coded	Sensitive	Handicapped	Others
1	Early debility, later fatigability				Acne, hair on lip	Schooling interrupted; always tired and exhausted	
2			? early neurologic lesion at 5		Stuttering		
3	White hair at 17				White hair		
4		Heart disease		Malnutrition, secondary anemia		Weak physique as child	
5	Hypothyroidism						Not specified
6				Strabismus			Not specified
7	Endocrine disorder				Strabismus; hair on face; obesity; scar on hand		
8					Slightly obese		
9	Anergic; delicate; never robust	Influenza	? encephalitis, endocrine disorder			Tired easily	
10	Strabismus		? heart disease		Strabismus	Easily fatigued; used physical handicaps to have school interrupted	
11					Appearance, too small		
12	Endocrine disorder				Weight (120 lbs.)		
13	Retinitis pigmentosa; deaf since 6	Hysterectomy		Rundown most of time	Deafness		
14	Anergic; easily fatigued		? anemia	Underweight; headaches		Easily fatigued; made most of symptoms	
15				Delicate; underweight			Not specified
16		Thyroid, hysterectomy			Leg deformed since 6	Worried about physical ailments	
17	Weak physique			Heart attacks; nausea; anemia		Used illness to have schooling interrupted	

The nature of the physical findings in these cases and the patients' reactions to them can be appreciated by a scrutiny of each individual case. All physical factors which were considered of possible or actual etiologic significance had been entered on the code sheet under the headings of constitutional anomalies, diagnosed physical disease and undiagnosed physical disease. These have been included in tables 16 and 17 as well as other physical factors which may be of significance in the development of the personality, although not coded.

The high incidence of such findings in these cases, 90.9 per cent, is even more significant when the group is compared with the general population. Figures given in the Second Report of the Provost Marshal General in 1919<sup>6</sup> on the United States Army Draft show that 29.6 per cent of the total number of men examined had physical defects, on the basis of which 2.8 per cent of the cases were classified as remediable, 10.6 per cent were qualified for limited service, and 16.2 per cent were disqualified. While these figures are not entirely comparable with ours, they may be used as a rough indication of how high these schizoid personalities run in physical defects.

The implications of these findings are of some interest in the light of what has been said by various writers on the subject who have pointed out the determinate rôle of physical handicaps in the development of morbid personality trends. Lee and Kenworthy in "Mental Hygiene and Social Work"<sup>7</sup> stated:

A great variety of common physical issues have become similarly involved in the personality and behavior problems that come to a child guidance clinic. Included among these we find eye and ear handicaps, nasal obstructions and disease, the many glandular disorders, dental abnormalities, tonsil and adenoid involvements, heart and lung affections, intestinal and bladder disorders, inadequate muscular development, paralyses, organic bony deformities, etc. In many of these cases the physical handicaps alone may produce an emotional over-loading for the child. They carry with them, especially for the intelligent sensitive child, a stigma of difference which sets him apart from his fellows on an undesirable plane and which, marking him as inadequate, is inevitably destructive. At times the handicap is not obvious yet operates by making normal adjustment difficult just as surely as does gross deformity. Eye defects which make academic work a burden, glandular defects which make energetic games exhausting, jaw formations which give queer twists and turns to speech, all contribute indirectly but incontestably to the development of emotional problems.

When the handicap is magnified by the attitudes of parents, teachers, competing brothers and sisters, schoolmates, and the like, the personality development is profoundly affected by the play of the environmental factors upon the structure and emotional development of the individual.

6. Second Report of the Provost Marshal General, U. S. Govt. Printing Office, 1919.

7. Lee, P. R., and Kenworthy, M. E.: *Mental Hygiene and Social Work*, The Commonwealth Fund, Division of Publications, New York, 1929, p. 93.

Amsden, in an article on "Mental and Emotional Components of the Personality in Schizophrenia," said:<sup>8</sup>

There are apparently other sources of this feeling of insecurity, such as actual physical or physiological handicap, which stands in the way of an assertion of the individual and places him at a disadvantage as compared with others.

Strecker and his collaborators<sup>9</sup> have described a "type with bodily inferiority. The individual with some physical defect . . . causing a shyness or shrinking from the world."<sup>7</sup>

While it is the theory of many writers that the presence of physical defects may bring out shyness, sensitivity and seclusiveness in the individual, there is still the possibility that our patients may be especially conscious of their defects because of a fundamental and inherent sensitivity. Certainly we can cite many cases in which a compensatory adjustment is made to a physical inferiority, with aggressiveness and self-assertion rather than withdrawal. The fact that we find among our patients instances of sensitivity over a supposed anomaly which might well be a source of satisfaction to other persons, such as a height of 6 feet and 2 inches (188 cm.) in a man or a weight of 120 pounds (54.4 Kg.) in a woman, raises the question whether these patients may not seize on a physical characteristic as an explanation for an original feeling of sensitivity.

*Sex Habits.*—The preoccupation with physical defects has been associated with sex practices by some writers. Levy, in a study of body interest in children and hypochondriasis,<sup>10</sup> stated:

Another source is represented by symptoms of the physiologic let-down resulting from excessive masturbation. These are chiefly in the form of lethargy, complaints of inappetence, lack of energy, and the like. And finally, there remain the symptoms of regression. In the retreat from reality, we have a situation that fosters introspection, increases sensitivity to all body sensations and limits sexual pleasure to autoerotic forms, thereby like a vicious circle raising the value of the retreat.

When frequent masturbation occurs they [hypochondriacal symptoms] appear to be built up in some cases on the physiologic let-down symptoms following masturbation and appear especially in cases showing schizoid reactions.

In our group of patients 11 were known to have masturbated, 4 to an excessive degree, and 7 to an average (less than twice a week)

8. Amsden, G. S.: Mental and Emotional Components of the Personality in Schizophrenia, *Proc. A. Research in Nerv. & Ment. Dis.*, 1925, New York, Paul B. Hoeber, Inc., 1928.

9. Strecker, E. A.; Appel, K. E.; Eyman, E. V.; Farr, C. B.; Lemar, N. C.; Palmer, H. D., and Smith, L. H.: The Prognosis in Manic-Depressive Psychosis, *Proc. A. Research in Nerv. & Ment. Dis.*, 1930, Baltimore: Williams & Wilkins Company, 1932.

10. Levy, D. M.: Body Interest in Children and Hypochondriasis, *Am. J. Psychiat.* **12**:295, 1932.

degree. It was known that there was a definite conflict due to auto-erotism in 9 patients, of which 5 were males and 4 females.

Other known sex practices included overt homosexuality in childhood in 3 patients, 1 of them a male and 2 of them females. Heterosexual adjustment is dubious in the majority of these patients. None of the males and only 4 of the females had married, 3 of them unhappily and 2 to men from twelve to fifteen years older than they. Three men only were known to have had heterosexual coitus. Two others had attempted sexual relations on only one occasion without enjoyment, as well as 1 female. In 2 cases female patients had been raped. Three males and 1 female had had love affairs which they were unable to bring to culmination by marriage, so that in each instance the other person married while waiting for our patient to make up his mind.

Seven males and 6 females were described as being uninterested in the opposite sex. Four males were interested in girls but never did anything about it, while 3 females desired to marry but had no opportunity and 3 others had some regrets because they were not popular with boys. It was known definitely that no sex practices had ever occurred among 4 patients, 1 male and 3 females. In 6 other cases information on sex habits was entirely lacking. On the whole, it would appear that the prepsychotic sex adjustment in these patients was unsatisfactory.

*Intelligence.*—Intellectual inferiority, unlike physical and sexual inadequacy, does not characterize the schizoid group. Eighteen of the patients were estimated to fall into the first quartile of intelligence, 12 into the second, 2 into the third and 1 into the fourth. The fact that 90.9 per cent of these patients showed average or superior intelligence would seem to be in keeping with similar findings of Amsden.<sup>8</sup>

As measured by school achievement, 8 of these patients had grammar school education or less, 12 went to high school, 6 were high school graduates, 4 went to business college, 1 went to college, 1 was a graduate mechanic and 1 was a college graduate. Intellectual inferiority was felt by 4 patients, of whom 2 were sensitive as to their shortcomings in school and 2 others were unable to achieve their ambitions because of lack of ability.

*Occupational Adjustment.*—In their work adjustment it was found that only 13 of our patients were efficient and valuable employees. Four had no interest or feeling of responsibility in holding a job; 3 changed jobs frequently; 3 found their work a source of worry, and 2 were unable to find any employment. In 11 cases dissatisfaction was felt with the job because of thwarted ambitions.

We have thus been able to trace some relationship between the schizoid personality and elements in the heredity, family situations, physical make-up, sex practices and occupational adjustment of persons

with such an endowment. To what extent these factors have contributed directly to the final breakdown of the patient, other than in molding or aggravating an especially vulnerable predisposition to mental instability, we cannot say.

*Precipitating Situation.*—In 13 of the cases a definite environmental situation precipitated the psychosis, while in 6 others an exciting cause was less clearcut, although demonstrable. If we correlate the occurrence of situations precipitating the psychosis with personality anomaly, we find, as did Strecker in "A Preliminary Study of the Precipitating Situation in 200 Cases of Mental Disease,"<sup>11</sup> that "an abnormal personality occurred with greater frequency in those patients whose mental illness came on without adequate exciting factors." This inference may be drawn from table 18, although it is not of statistical significance.

TABLE 18.—*Precipitating Situation*

Precipitating Situation	Personality Anomaly			Total
	Present	Questionable	Not Specified	
Present.....	3	4	6	13
Doubtful.....	3	1	2	6
Absent.....	13	1	0	14
	19	6	8	33

## CONCLUSIONS

1. The aim of this study was to answer two questions: (a) Do patients with similar schizoid personalities have similar clinical pictures when they break down? (b) Can the schizoid personality be described in terms of a given constellation of traits?

2. We have arbitrarily defined the schizoid personality as possessing five characteristics: few friends, shyness, seclusiveness, close-mouthedness and extreme sensitivity.

3. Only 33 of 327 patients with all diagnoses were found to have had this combination of traits in prepsychotic life; 24 of these had schizophrenia, out of a total of 151 with schizophrenia.

4. The clinical picture presented in these cases varied greatly from case to case with only slight superficial resemblances.

5. In spite of the allegedly unfavorable constellation of traits in the schizoid personality, the recovery rate was higher than in an unselected group of schizophrenic patients or in general hospital populations.

6. Analysis of factors favoring recovery did not reveal any single especially significant condition in all cases.

11. Strecker, E. A.: A Preliminary Study of the Precipitating Situation in 200 Cases of Mental Disease, *Am. J. Psychiat.* **1**:503, 1922.

7. Of the 33 patients with schizoid personalities, the males were admitted to the hospital on the average ten years earlier than the females, pointing to certain conditions in our culture that lead to the hospitalization of maladjusted males at an earlier age than females.

8. Only 15.9 per cent of all the schizophrenic persons in the research had the specific combination of traits which we outlined as delineating the schizoid personality. These traits, however, were singly most commonly found in the schizophrenic group, together with "neurotic traits," "model child," "close attachment to the family," "little self-assertiveness," "frequent day-dreaming," "great ambition," "total abstainers" and nonsmokers.

9. Significantly associated with the nucleus of five traits which we selected were "little self-assertiveness," "no sense of humor," "frequent day-dreaming," "little output of energy," "feeling of inferiority," "fusses over pain," "very absent-minded," "regular church-goers," "nonsmokers," "total abstainers," "neurotic traits" in childhood and "unusual attachments" to some member of the family, in adult life.

10. It was noted that, in the transition from childhood to adult life, the neurotic traits decreased noticeably in the schizoid group, while practically all other schizoid traits increased.

11. The five traits which we assumed to be basic in the schizoid personality are not unitary traits but can be readily split into other functional components.

12. A review of various clinical data reveals that the most frequent factors associated with the schizoid personality are overattachment to the family, maternal overprotection, paternal neglect, physical defects and anomalies present in practically all of the cases and unsatisfactory heterosexual adjustments.

13. Finally, we believe that a description of the schizoid personality by traits does not give a true picture of the personality or of its dynamic relation to the psychosis.

## THE BLOOD CHOLESTEROL IN SCHIZOPHRENIA

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The claim that cholesterol metabolism is disturbed in patients suffering from schizophrenia has frequently been made by investigators in this field. The fact that approximately 50 per cent of the brain is made up of lipid constituents has led naturally to the question whether patients showing mental disturbances would not also show changes in cholesterol metabolism. Despite the fact that cholesterol was one of the first substances for which a specific color reaction was developed, accurate colorimetric procedures for its determination were made available only recently. Variations in the level of the blood cholesterol have been ascribed to changes in emotion and to disturbances of the endocrine glands, especially the thyroid gland, the suprarenals and the gonads. Unfortunately, the conclusions reached by various workers are contradictory.

### PREVIOUS STUDIES

Low values (less than 140 mg. per hundred cubic centimeters of blood) were recorded in dementia praecox by Pighini,<sup>1</sup> Gibbs,<sup>2</sup> Parhon and Parhon,<sup>3</sup> Shaw and Sharpe,<sup>4</sup> Stenberg,<sup>5</sup> Ornstein<sup>6</sup> and Forsythe.<sup>7</sup> High values (above 200 mg.) were given by Pighini,<sup>1</sup> Parhon, Urechia and Popea,<sup>8</sup> Goebel<sup>9</sup> and Duncan.<sup>10</sup> Normal values (between 140 and 200 mg.) were reported by de Crinis,<sup>11</sup> Targowla, Badonnel and Berman<sup>12</sup> and Jacobi.<sup>13</sup>

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From the Memorial Foundation for Neuro-Endocrine Research, with the collaboration of the Research Staff of the Worcester State Hospital.

1. Pighini, G.: *Ztschr. f. d. ges. Neurol. u. Psychiat.* **4**:629, 1911.
2. Gibbs, C. E.: *Am. J. Psychiat.* **5**:189, 1925.
3. Parhon, C. J., and Parhon, M.: *Encéphale* **22**:48, 1925.
4. Shaw, B. H., and Sharpe, J. S.: *J. Ment. Sc.* **77**:53, 1931.
5. Stenberg, S.: *Acta med. Scandinav.* **71**:558, 1921; **72**:1, 1929.
6. Ornstein, I.: *Compt. rend. Soc. de biol.* **93**:1622, 1925.
7. Forsythe, W. L.: *J. Ment. Sc.* **72**:219, 1926.
8. Parhon, C. J.; Urechia, C., and Popea, A.: *Ztschr. f. d. ges. Neurol. u. Psychiat.* **7**:1021, 1913.
9. Goebel, F.: *Folia clin. et biol.* **1**:110, 1927.
10. Duncan, A. G.: *J. Ment. Sc.* **76**:284, 1930.
11. de Crinis, M.: *Ztschr. f. d. ges. Neurol. u. Psychiat.* **78**:42, 1922.
12. Targowla, R.; Badonnel, M., and Berman, A.: *Encéphale* **18**:138, 1923.
13. Jacobi, W.: *Monatschr. f. Psychiat. u. Neurol.* **62**:296, 1926.

As Stenberg has given an excellent summary of the literature, only the more important of the previous investigations will be discussed.

Pighini,<sup>1</sup> in 1911, published the results of an investigation of the serum cholesterol in 83 patients, including 11 males with dementia praecox. He used his own method, which required 200 cc. of blood, so that each sample had to be collected over a ten day period. Six of the patients with chronic dementia praecox had values from 70 to 135 mg.; the remaining 3 patients with chronic cases gave values from 269 to 440 mg., and the 2 patients with acute dementia praecox gave values of 328 to 508 mg. As the method involves weighing the extracted cholesterol, it is questionable whether much reliance can be placed on the results.

In 1925, Gibbs,<sup>2</sup> using Bloor's<sup>14</sup> method, obtained as average values for the whole blood cholesterol of male patients with dementia praecox 113.7 mg. in 11 patients who showed emotional deterioration, 106 mg. in 4 patients with acute cases, and 149.5 mg. in 6 patients who showed no evidence of deterioration.

In 1929, Stenberg,<sup>3</sup> using Bang's method, made a careful statistical analysis of blood cholesterol values in patients with manic-depressive psychosis and dementia praecox. In 62 women he obtained a mean value of  $163 \pm 4$  mg. and a standard deviation of 33.5 mg., as compared with a mean value of  $153 \pm 3$  mg. and a standard deviation of 16 mg. in his female controls. In 15 male patients the mean cholesterol value was  $138 \pm 7$  mg., with a standard deviation of 28.9 mg., and in 9 male controls there was a mean value of  $144 \pm 6$  mg., with a standard deviation of 17 mg. He concluded that there is no significant difference between the blood cholesterol values in patients with dementia praecox and in normal persons. He also concluded that there is a clearly demonstrable relation between cholesterol and emotional tone, since 94 per cent of the patients with cholesterol values above 170 mg. showed heightened emotional tone, and 100 per cent of those with values below 130 mg. showed dulness.

In contrast to these findings, Duncan,<sup>10</sup> in 1930, stated that patients with dementia praecox when in dull or quiet mental states have high serum cholesterol values. He found an average content of 214 mg. in 76 patients, 47 of whom showed supranormal figures. In states of confusion or excessive emotion the content was much lower, averaging 179 mg. in 38 patients. Of 25 patients on whom repeated analyses were made, 21 gave lower values during periods of excitement than in the intervals of quiet or apathy. The average figures for the 25 patients were 224 mg. per hundred cubic centimeters of serum during the quiet intervals and 185 mg. during periods of excitement.

14. Bloor, W. R.; Pelkan, K. F., and Allen, D. M.: *J. Biol. Chem.* **52**:191, 1922.

The values given in 1931 by Shaw and Sharpe<sup>4</sup> are the lowest recorded for patients with dementia praecox. These authors obtained an average value of 51.6 mg. per hundred cubic centimeters of whole blood in a series of 10 cases. Four patients had values between 30 and 35 mg., and the highest value was only 85 mg. These results are so extremely low and at such variance with other values recorded in the literature that one is led to suspect the possibility of faulty technic. The fact that the authors recorded blood urea values obtained by the obsolete hypobromite method does not tend to strengthen one's belief in the validity of the figures for cholesterol.

Many attempts have been made to show a correlation between the basal metabolic rate and the cholesterol content of the blood. Epstein and Lande,<sup>15</sup> Werner,<sup>16</sup> Shapiro<sup>17</sup> and Mason, Hunt and Hurxthal<sup>18</sup> maintained that there is an inverse relation between the cholesterol level of the blood and the basal metabolic rate. This was denied by Luden,<sup>19</sup> Wade,<sup>20</sup> Grabfield and Campbell<sup>21</sup> and Gardner and Gainsborough.<sup>22</sup> Duncan<sup>23</sup> reported that the administration of thyroid causes a rapid lowering of the blood cholesterol. Seven patients with dementia praecox, with an average cholesterol value of 258 mg. per hundred cubic centimeters of serum, had an average value of 139 mg. after thyroid medication.

The lack of agreement as to the cholesterol content of the blood may be explained in part by the great variation in the same person in the course of a few hours and the wide range in normal persons, as well as by variation in methods. In some cases a suspicion of technical incompetence may be entertained. Considerable variation is noted in reports on normal subjects. Patterson,<sup>24</sup> using Bloor's method on five medical students, obtained an average value of 197 mg. per hundred cubic centimeters of whole blood, and a range of from 169 to 210 mg.

15. Epstein, A. A., and Lande, H.: Studies on Blood Lipoids: Relation of Cholesterol and Protein Deficiency to Basal Metabolism, *Arch. Int. Med.* **30**:563 (Nov.) 1922.

16. Werner, G.: *Compt. rend. Soc. de biol.* **100**:928, 1929.

17. Shapiro, S.: *J. Exper. Med.* **45**:595, 1927.

18. Mason, R. L.; Hunt, H. M., and Hurxthal, L. H.: *New England J. Med.* **203**:1273, 1930.

19. Luden, G., in *Collected Papers of Mayo Clinic*, Philadelphia, W. B. Saunders Company, 1918, vol. 10, p. 482.

20. Wade, P. A.: *Am. J. M. Sc.* **177**:790, 1929.

21. Grabfield, G. P. and Campbell, A. G.: *New England J. Med.* **205**:1148, 1931.

22. Gardner, J. A., and Gainsborough, H.: *Brit. M. J.* **2**:935, 1928.

23. Duncan, A. G.: *J. Ment. Sc.* **77**:332, 1931.

24. Patterson, J. W. T.: *Biochem. J.* **21**:958, 1927.

Gardner and Gainsborough<sup>25</sup> reported a mean value of 170 mg. per hundred cubic centimeters of plasma for men, and a range of from 110 to 220 mg. One man, on whom analyses were made at intervals during three years, gave a value of 190 mg. at the beginning and 200 mg. at the end of that time, although he showed a fluctuation from 170 to 226 mg. in one month. Stenberg<sup>6</sup> gave the average value for 9 normal men as 144 mg., with a standard deviation of  $\pm 17$  mg.

Robinson, Brain and Kay,<sup>26</sup> using Sackett's modification of Bloor's method on 39 men, obtained a mean value of 172 mg. per hundred cubic centimeters of whole blood, with limits of 157 and 222 mg., and a mean value of 163 mg. per hundred cubic centimeters of plasma, with limits of 142 and 212 mg. These results are at variance with the consensus that whole blood contains proportionately a slightly lower amount of cholesterol than does plasma. They also reported that in 8 medical students the average cholesterol content of the whole blood fell from 190 mg. to 168 mg. immediately after exercise. This is a contradiction of the results of Patterson,<sup>24</sup> who found no significant change after exercise.

Oser and Karr,<sup>27</sup> using the method of Myers and Wardell,<sup>28</sup> in 18 normal persons found a mean value of 187 mg. per hundred cubic centimeters of plasma, with limits of 105 and 261 mg., and a mean value of 154 mg. per hundred cubic centimeters of whole blood, with limits of 110 and 190 mg.

Friedlander and Silbert,<sup>29</sup> using Sackett's modification of Bloor's method, obtained an average value for the plasma cholesterol of 13 normal persons of 165 mg., with limits of 135 and 185 mg.

Rabinowitch,<sup>30</sup> using Bloor's method, made 314 determinations of plasma cholesterol in a group of diabetic patients with normal blood sugar and sugar-free urine. He obtained a mean value of 184 mg. and a standard deviation of 57 mg.

McEachern and Gilmour<sup>31</sup> reported an intensive study of the blood cholesterol values in 28 normal persons (sex not given), using the method of Bloor, Pelkan and Allen.<sup>14</sup> They obtained a mean value of 156 mg., with a range of from 135 to 193 mg. The greatest individual

25. Gardner, J. A., and Gainsborough, H.: *Biochem. J.* **21**:130, 1927; **22**:1048, 1928.

26. Robinson, S. H. G.; Brain, W. R., and Kay, H. D.: *Lancet* **2**:325, 1927.

27. Oser, B. L., and Karr, W. G.: *Lipoid Partition in Blood in Health and Disease*, *Arch. Int. Med.* **36**:507 (Oct.) 1925.

28. Myers, V. C., and Wardell, B. L.: *J. Biol. Chem.* **36**:147, 1918.

29. Friedlander, M., and Silbert, S.: *Thrombo-Angiitis Obliterans (Buerger)*, *Arch. Int. Med.* **48**:500 (Sept.) 1931.

30. Rabinowitch, I. M.: *The Cholesterol Content of Blood Plasma in Diabetes Mellitus*, *Arch. Int. Med.* **43**:363 (March) 1929.

31. McEachern, J. M., and Gilmour, C. R.: *Canad. M. A. J.* **26**:30, 1932.

variation was 84 mg. in two hours, from 218 mg. to 134 mg., and the smallest variation in five hours was 25 mg., from 170 to 195 mg.

Similar fluctuations in the cholesterol content of the blood were obtained by Bruger and Somach,<sup>32</sup> using the method of Myers and Wardell.<sup>28</sup> They reported that the taking of food has little or no effect on the blood cholesterol, and that all determinations of cholesterol

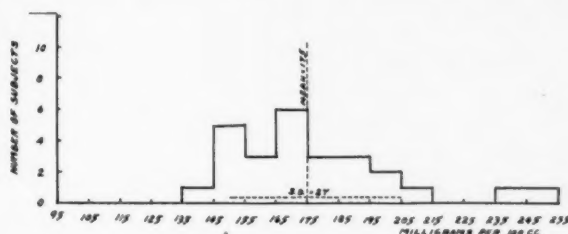


Chart 1.—Values for whole blood cholesterol in 26 normal men. S. D. indicates standard deviation.

TABLE 1.—Blood Cholesterol in Normal Human Subjects

Investigator	Mean Value Whole Blood, Mg. per 100 Cc.	Mean Value Plasma, Mg. per 100 Cc.	Range, Mg. per 100 Cc.	Number Patients	Sex	Method
Patterson .....	197	...	169-210	5	M	Bloor
Gardner and Gainsborough....	...	170	110-220	6	M	Fex
Stenberg .....	144	...	93-196	9	M	Bang
	153	...	105-201	25	F	Bang
Robinson, Brain and Kay.....	172	...	157-222	30	M	Bloor
Oser and Karr.....	...	187	105-261	18	M ?	Myers
	154	...	110-190	18		
McEachern and Gilmour.....	161	...	130-218	28	F ?	Bloor
Friedlander and Silbert.....	...	165	135-185	13		
Bruger and Somach.....	...	216	191-250	4	M	Myers
Gray and McGee.....	194	...	155-234	20	..	Bloor
		216		20		
Looney and Childs.....	175	...	142-250	26	M	Myers
Weighted grand mean.....	169					

should be made in the morning as the blood taken at this time shows smaller variations. They obtained a mean value of 216 mg. per hundred cubic centimeters of plasma, and a variation of from 15 to 48 mg. in 4 normal men. Gray and McGee,<sup>33</sup> using the method of Bloor, confirmed these results. In 29 controls (sex not given), they obtained for whole blood a mean value of  $194 \pm 2.7$  mg., with a standard deviation

32. Bruger, M., and Somach, I.: J. Biol. Chem. **97**:23, 1932.

33. Gray, H., and McGee, L. C.: Cholesterol Content of Blood in Epilepsy and in Feeble-mindedness, Arch. Neurol. & Psychiat. **28**:357 (Aug.) 1932.

of 22 mg. and a coefficient of variation of 11.5 per cent. For plasma, the mean for 20 persons was  $216 \pm 6.4$  mg.

In connection with the study on schizophrenic subjects, we made determinations on whole blood from 26 male physicians, medical students and laboratory workers. These results are given in chart 1. The mean cholesterol value was  $175 \pm 5.3$  mg., with a standard deviation of 27 mg. and a coefficient of variation of 15 per cent. The range was from 142 to 250 mg.; 24 of the 26 men gave figures below 212 mg. This mean value agrees well with that of 172 mg. given by Robinson, Brain and Kay<sup>26</sup> for 39 men, as well as with the average of all the results reported (shown in table 1). The mean value for 179 persons, studied in ten laboratories, regardless of sex, was 169 mg. per hundred cubic centimeters of whole blood.

Values of 140 and 225 mg. per hundred cubic centimeters may be taken as arbitrary limits for normal whole blood cholesterol.

#### METHODS

In our studies the determinations were made by the method of Myers and Wardell<sup>28</sup> on whole blood taken in the morning, during fasting. The patients were all men suffering from dementia praecox; with few exceptions they were between the ages of 20 and 45.

During the first month of the seven months' study<sup>34</sup> determinations of cholesterol were made in the first and third weeks. These were repeated in the fourth and also in the seventh month.

#### RESULTS

In the first period of our study 67 determinations were made on 37 patients; for 7 cases only one analysis was obtained. The mean value was  $147 \pm 3.3$  mg.<sup>35</sup> per hundred cubic centimeters of whole blood, with a standard deviation of 27 mg. The minimum value was 91 mg., and the maximum, 207 mg., giving a range of 116 mg. This is shown in chart 2.

In the second period, 109 determinations were made on 57 patients. The frequency distribution of all the values is shown in chart 3. The mean value was  $162 \pm 3.3$  mg., and the standard deviation, 26 mg. The minimum value was 95 mg., and the maximum, 270 mg., giving a range of 175 mg.

34. The so-called seven months' study consisted of an extensive investigation of a large number (163) of physiologic and psychologic variables in 72 male patients. These variables were determined during the first, fourth and seventh months of the study, with rest periods of two months between repetitions of the examinations (Hoskins, R. G.: *J. Nerv. & Ment. Dis.* **75**:663, 1932; Oxygen Consumption ["Basal Metabolic Rate"] in Schizophrenia, *Arch. Neurol. & Psychiat.* **28**:1346 [Dec.] 1932).

35. Throughout this paper our figures refer to the standard error.

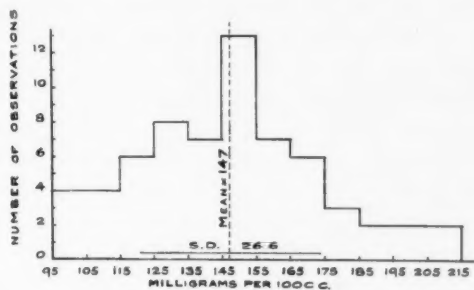


Chart 2.—Frequency distribution of cholesterol values; all values, first period.

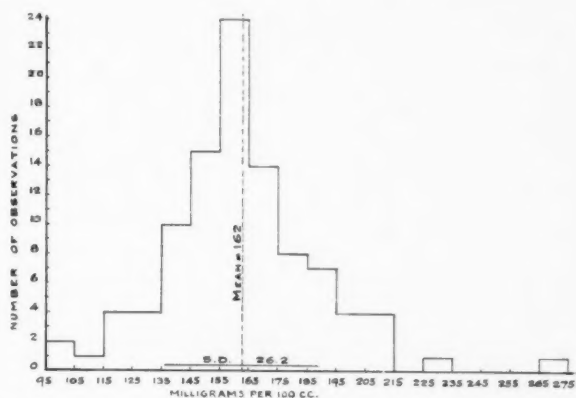


Chart 3.—Frequency distribution of cholesterol values; all values, second period.

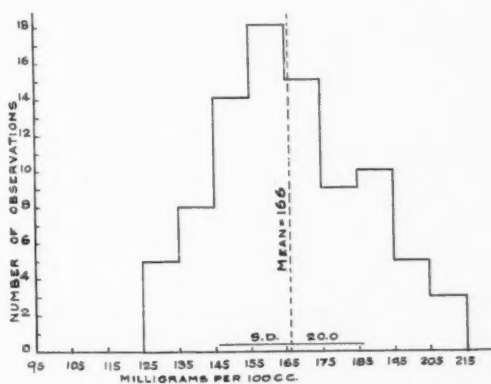


Chart 4.—Frequency distribution of cholesterol values; all values, third period.

In the third period, 87 determinations were made on 45 patients. The results are shown in chart 4. The mean was  $166 \pm 2.5$  mg., and the standard deviation, 20 mg. The minimum value was 129 mg., and the maximum, 211 mg., giving a range of 82 mg.

The mean value obtained during the first period was 15 mg. greater than that for the second. From the second to the third period there was an increase of 5 mg.

These differences are not to be ascribed to errors in technic. The greatest precautions were taken to prevent overheating at any stage,

TABLE 2.—Duplicate Analyses of Whole Blood Cholesterol

Subject	Cholesterol, Mg. per 100 Cc.	Subject	Cholesterol, Mg. per 100 Cc.	Subject	Cholesterol, Mg. per 100 Cc.
J. A.....	139	A. J.....	159	C. M.....	146
	139		151		148
	138		149	A. T.....	175
	143	A. B.....	141		183
H. H.....	161		143	A. H.....	189
	161	A. B.....	149		181
	158		147	F. P.....	225
A. J.....	182		148		233
	183	M. T.....	152	W. R.....	172
E. O.....	155		152		175
	154	A. B.....	135	A. D.....	177
P. S.....	154		133		179
	160	A. B.....	143	G. P.....	207
J. A.....	147		136		211
	148	B. C.....	170	H. F.....	245
H. H.....	165		178		239
	167	A. B.....	153	H. F.....	238
E. O.....	163		163		231
	163	A. L.....	197	R. S.....	164
A. B.....	138		198		161
	141	T. G.....	181	E. G.....	181
J. P.....	153		181		179
	148		179		
F. P.....	168				
	156				

Mean of the differences,  $3.6 \pm 0.5$  mg.;  $\sigma$ , 3.1 mg.

the introduction of the slightest trace of water or incomplete extraction of cholesterol. All the chloroform used was redistilled after shaking with anhydrous calcium chloride, and the extractions were run for a period of ninety minutes instead of thirty as directed by the authors of the method. During the extraction the flasks were carefully watched to prevent them from becoming dry. The drying of the calcium sulphate was carried out below 105 C. and any experiment in which there was any reason to suspect overheating was repeated. In all instances in which the value was below 140 mg. the determination was repeated.

The error which can be ascribed to analytic technic is given in table 2, which shows the results of multiple analyses on 32 samples. From the results of these analyses it will be noted that the mean difference

between determinations made on the same sample of blood is  $3.6 \pm 0.5$  mg., a value that is probably as low as can be obtained by the method used.

In the second period 14 per cent of the patients had values below 140 mg., which we have taken as the lower limit of normal; only 2 patients had values above 215 mg.

In the third period only 9 per cent of the patients showed hypocholesterolemia and not a single value above 215 mg. was obtained.

While the mean value increased in each successive period, the relative variation decreased constantly and the distributions became more and more compact and symmetrical.

The mean range for individual patients for periods of two weeks was about 20 mg., and for the entire seven months, 44 mg.

Our results bear out those of other investigators in showing that the cholesterol content of whole blood can fluctuate widely from time to time. Usually a difference as great as 40 mg. can be expected in determinations made at different times on the blood of the same patient taken under identical conditions. Analyses made within five hours may show a variation of 80 mg., while those made after six months may agree within 5 mg.

Consistently high normal values were shown by only 1 patient, who gave values above 200 mg. but below 215 mg. in every test. Another patient gave values of 270, 268, 203 and 179 mg. None of the patients had consistently low values, and only 1 had 3 low readings in 6 determinations, namely, 102, 116 and 129 mg., the other 3 being in the low normal range (155, 157 and 163 mg.).

When the patients were studied by subgroups it appeared that there was no significant difference in the mean cholesterol values, except that the hebephrenic group gave a somewhat lower value (average, 154 mg.) than the others.

Our schizophrenic patients tended to have a lower blood cholesterol content than the controls. This difference was marked in the first period. In the next two periods the differences were less marked, being barely significant in the second period and not significant in the third period. The average for the schizophrenic patients for the three periods was 17 mg. below that of the controls.

The analyses for the first period were carried out during August, September and October; those for the second period, during November, December and January, and those for the last period, during February, March and April. It is possible, therefore, that the difference between the first period and the later periods is due to a seasonal factor. As the analyses of the blood specimens from the normal controls were made during the last period, such a seasonal variation would accentuate the difference between the normal values and those for the first period.

It is to be noted that the cholesterol values for individual patients, on the whole, fall within the normal limits, although the greater number tend to be grouped at the lower levels. For this reason the mean of a large series of observations on schizophrenic patients will be lower than that for normal persons.

Recently, Hoskins<sup>36</sup> suggested that schizophrenia is characterized by homeostasis on levels displaced somewhat from those usually observed in normal persons. In this study we appear to have confirmation of this idea so far as it applies to cholesterol.

In order to find out whether there is any relationship between the basal metabolic rate and the level of blood cholesterol, as suggested by the investigators previously cited, the values for blood cholesterol in

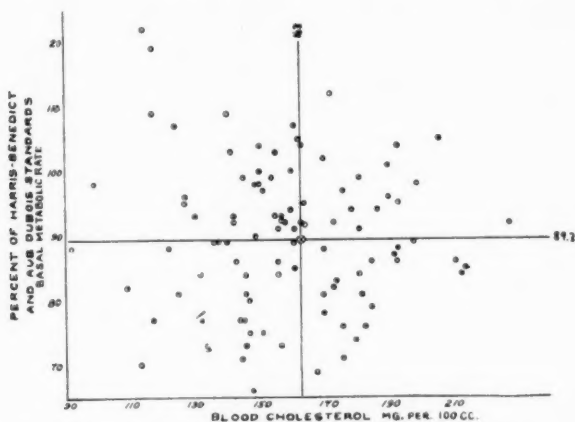


Chart 5.—Basal metabolic rate versus blood cholesterol; all observations. The symbol (cross within a circle) marks the intersection of the mean basal metabolic rate, 89.3 per cent, and the mean cholesterol value, 163 mg.

milligrams per hundred cubic centimeters were plotted as abscissas against the basal metabolic rates as ordinates. The blood for the determinations of cholesterol was taken immediately after the completion of the determinations of the basal metabolic rate. Only those determinations of basal metabolism were included in which the patient was in a satisfactory basal state. The results of 100 separate observations were plotted in a scatter diagram, shown in chart 5. It will be seen that there is no relationship between the blood cholesterol and the basal metabolic rate. The points fall evenly on all sides of the point of intersection of the mean basal metabolic rate of 89.3 per cent and the mean cholesterol value of 163 mg. per hundred cubic centimeters. It should

36. Hoskins, R. G.: Analysis of Schizophrenia Problem from Standpoint of Investigator, *J. A. M. A.* **97**:682 (Sept. 5) 1931.

be indicated, however, that Mason, Hunt and Hurxthal<sup>18</sup> dealt with a group of patients who showed much greater variation in basal metabolic rate than did those in our series. Our results agree with those reported by Grabfield and Campbell,<sup>21</sup> although these authors had a few cholesterol figures much higher than any that we obtained.

From these results we may state that for basal metabolic rates falling between 60 and 130 per cent of normal there is no correlation with the blood cholesterol in men with schizophrenia.

As previous investigators (Stenberg,<sup>5</sup> Duncan<sup>10</sup>) had reported contradictory results in the correlation of emotional states with cholesterol values, we tested the relationship by means of contingency tables. In previous studies the entire work was performed by the same investigator, who not only rated the emotional states of the patients but carried out the analytic procedures and made the correlations. In this study the analytic determinations were made by one worker; the rating of the emotional status of the patients was made on the same day by a psychiatrist who was unacquainted with the biochemical phase of the work, and the correlations were made by a statistician, working independently.

Careful analysis of our results failed to reveal any correlation between these two variables.

When the number of agitated and nonagitated patients is plotted against different values for cholesterol in a contingency table, the  $\chi^2$  for this table is 3.83, and the probability that the differences observed could occur from irregularities in sampling lies between 0.3 and 0.2. As a *p* value of less than 0.05 is required by most statisticians in order to show association, no association was demonstrated in our series.

We have also tested for correlation by recording the changes in the cholesterol values from the second to the third period against the changes in emotional status for the same interval. No set value is given as high, but the minimum reading for each patient is designated as low. Here we have four degrees of freedom and obtain a  $\chi^2$  of 6.82 and a corresponding probability of chance occurrence of between 0.1 and 0.2. If change in emotional tone results in change in the blood cholesterol, such changes should show a high degree of correlation by this method, regardless of the level of the cholesterol. We were unable to detect any such correlation.

#### COMMENT

The mean value of the whole blood cholesterol for all three periods was 158 mg. per hundred cubic centimeters. This value is somewhat lower than the grand mean for normal persons recorded in table 1 (169 mg.). This grand mean includes determinations made by several methods and is undoubtedly lower than it would have been if all the investigators had used the method of Myers and Wardell,<sup>28</sup> which gives

higher values. For this reason it would seem that we should use for comparison of schizophrenic and nonpsychotic subjects the mean value of 175 mg. obtained in our own study of normal persons.

The difference between mean value for our schizophrenic patients and that for the controls is 17 mg., which is a significant decrease, as a value of only 14.1 mg. is needed for a statistically valid difference. However, if we compare the results for each period, only the first period shows a significant change. The discrepancy between the values for this period and those for the last two periods requires explanation. As already stated, it is unlikely that the difference is due to errors in analytic technic; and it would seem to be due to a seasonal variation. On the basis of the present study we are unable to determine this point positively, and we shall carry the investigation further.

Though the average blood cholesterol values for a series of schizophrenic patients is somewhat lower than that for normal persons, the cholesterol content for a given patient cannot be used as an aid in the diagnosis of schizophrenia, since the variability is so great and the range is so wide that no single determination can be taken as characteristic. The great variability of the cholesterol content in our patients as well as in normal persons seems to indicate that simple determinations of the cholesterol content of the blood are worthless as clinical aids except in extreme conditions.

Most of the conclusions drawn from the results of investigations recorded in the literature must be revised in the light of present knowledge of the variability of the cholesterol of the blood. No reliance can be placed on isolated determinations or on analyses in a few cases.

This variability was pointed out by McEachern and Gilmour<sup>31</sup> who in 28 normal, fasting persons found variations of from 25 to 80 mg. in the cholesterol content of the blood during a period of five hours. Bruger and Somach<sup>32</sup> reported the same inconstancy of blood cholesterol values, although their variations were smaller, the largest being 48 mg.

As the increases in the cholesterol content of the blood taken at intervals after feeding do not exceed those found in fasting states, it is not permissible to postulate, as some writers have done, that cholesterol is concerned in the absorption and transportation of fat.

It is probably due to the variability in the cholesterol content of the blood that contradictory effects on the cholesterol level have been reported after the removal of the spleen or suprarenal glands. No change in the cholesterol level after suprarenalectomy was found by Baumann and Holly<sup>37</sup> or by Randles and Knudson,<sup>38</sup> while an increase was found

37. Baumann, E. J., and Holly, O. M.: *J. Biol. Chem.* **55**:457, 1923.

38. Randles, F. S., and Knudson, A.: *J. Biol. Chem.* **76**:89, 1928.

by Joelson and Shorr.<sup>39</sup> After splenectomy Bloor and MacPherson<sup>40</sup> found an increase, but Bodansky<sup>41</sup> and Randles and Knudson<sup>38</sup> found no change.

The significance of the increased blood cholesterol values in patients with severe cases of diabetes is not open to the same objection. In the first place, the increase in such cases may be extreme, e. g., from 800 to 1,500 mg., and in the second place, the variability at the higher levels is much less than at the lower levels.

Exercise has been said by Robinson, Brain and Kay<sup>26</sup> to cause a decrease in the blood cholesterol. This finding is open to the objection that 8 cases are not sufficient to establish such a relationship, in view of the known variability of the cholesterol content. Moreover, Patterson<sup>24</sup> was unable to obtain any significant change.

#### SUMMARY

Approximately 50 men with schizophrenia were studied over a period of seven months at intervals of two weeks and of three months. The cholesterol content of the whole blood was determined by the method of Myers and Wardell.<sup>28</sup> The mean cholesterol values were:  $146 \pm 3$  mg. per hundred cubic centimeters for the first period,  $161 \pm 2.8$  mg. for the second period, and  $166 \pm 2.5$  mg. for the third period.

The mean value for 26 normal men was  $175 \pm 5.2$  mg. Both the schizophrenic patients and the controls showed great variability in the cholesterol values, the former having a standard deviation of about 20 mg., and the latter, of 27 mg.

The difference between the mean value for the first period and those for the last two periods is believed to be due to a seasonal variation in the cholesterol content of the blood.

No correlations could be shown between the blood cholesterol and the basal metabolic rate or the emotional status.

Schizophrenia seems to be characterized by a slight degree of depression of the cholesterol content of the blood.

39. Joelson, J. J., and Shorr, E.: Relation of Suprarenals to Cholesterol Metabolism, *Arch. Int. Med.* **34**:841 (Dec.) 1924.

40. Bloor, W. B., and MacPherson, D. J.: *J. Biol. Chem.* **31**:79, 1917.

41. Bodansky, M.: *J. Biol. Chem.* **58**:239, 1925.

## OPTIC PSEUDONEURITIS AND PSEUDOPAPILLEDEMA

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AND

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The decision as to whether an eyeground is pathologic or normal is not always simple. Just as slight pallor of the optic disks does not necessarily mean early optic atrophy, so there are degrees of redness of the nerve heads, blurring of their margins and even measurable elevation of the disk which do not signify a pathologic condition, but which may confuse the observer.

Normal nerve heads which are red and elevated and which appear to have many of the characteristics of either optic neuritis or papilledema are occasionally encountered. In the past, all such nerve heads have been grouped together as pseudoneuritis. We believe that a more accurate classification will be of value for the recognition and understanding of the phenomenon.

We were able to find only ten cases of pseudoneuritis reported in the literature of the past decade. This does not include instances of unusual appearances of the nerve heads noted in other conditions. Several of the cases were recorded because of a more or less serious mistake in diagnosis. In a case reported by Taylor,<sup>1</sup> in a boy aged 11½ years, the appearance of the disks led to a diagnosis of a tumor of the brain. The patient was observed for seven years, during which time there was no change in the appearance of the nerve heads. Dunphy<sup>2</sup> described two cases in which it was a matter of the greatest difficulty to tell whether or not the condition was true papilledema.

The cases of pseudoneuritis not reported as such but noted incidentally occurred for the most part in the presence of marked refractive errors.<sup>3</sup> Three cases were reported by Reese<sup>4</sup>—one associated with hyperopia and one with myopia and one in which the refraction was not recorded.

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Read at a meeting of the New York Neurological Society, March 7, 1933.

From the Ophthalmological and Neurological Services of the Mount Sinai Hospital.

1. Taylor, J.: *Brit. J. Ophth.* **12**:378, 1928.
2. Dunphy, E. B.: *Am. J. Ophth.* **12**:834, 1929.
3. Crisp, W. H., and Shields, J. M.: *Am. J. Ophth.* **10**:629, 1927. Lambert, R. K., and McDannald, C. E.: *Am. J. Ophth.* **14**:46, 1931.
4. Reese, W. S.: *Am. J. Ophth.* **8**:492, 1925; **11**:900, 1928.

In 1928, de Schweinitz<sup>5</sup> offered the first classification of pseudoneuritis, which he based on both the appearance of the nerve heads and the etiology. He suggested the four following groups.

1. Pseudoneuritis associated with eye-strain, the nerve heads appearing red or grayish red, with blurred margins.
2. Pseudoneuritis of a permanent congenital form, with congenital vascular anomalies and a gray areola around the disk.
3. A pseudopapilledema, in which the disk is covered by a layer of transparent injected and edematous tissue, perhaps congenital.
4. A congenital and familial type of choked disk; similar in appearance to subsiding papillitis or papilledema.

In our experience, by far the most common variety of pseudoneuritis is that which is encountered in the presence of marked refractive errors, particularly those of a hyperopic or astigmatic nature. The part that eyestrain plays in the production of the condition is, however, not clear to us. We have made no particular effort to collect examples of this type, as we consider it a well established entity. The hyperemic nerve head usually seen has a fairly characteristic appearance and is frequently distorted by the astigmatism present. It is regarded with composure by most ophthalmologists.

The second group of cases is apt to be somewhat more confusing than the first. These cases, however, are recognizable morphologically by the obviously congenital anomalies present, especially those of the blood vessels. We have followed two patients with this type of pseudoneuritis for four years and one year respectively, and we shall submit their histories.

We include the cases which fall into the last two subdivisions of de Schweinitz' classification in one group. Observers of cases in this group are by no means in agreement as to the innocent nature of the picture of the fundi. Three cases, however, in each of which the condition closely resembled papilledema, have been observed for three years, fourteen months and two years respectively, and as yet no evidence of an active pathologic condition has been disclosed.

We have followed all our cases except one not only by the routine procedures and by frequent ophthalmoscopic examinations, but by taking photographs of the fundi from time to time and by plotting the blind spots and angioscotomas. The photographs were taken with a Zeiss-Nordenson retinal camera.

Examination of the blind spots should be made by all who study changes in the optic nerve. A definite relationship between the size of the blind spots and the degree of papilledema was demonstrated by

5. de Schweinitz, G. E.: *Am. J. Ophth.* **11**:985, 1928.

Davis<sup>6</sup> in a comprehensive study of one hundred and fifty cases. He stated that the studies, made both preoperatively and postoperatively, revealed changes in the size of the blind spots corresponding to the intracranial pressure. He believed this finding to be of greater significance than the degree to which the disk was elevated, possibly because the elevation is difficult to determine accurately and is a matter concerning which ophthalmologists frequently differ.

The blind spots can be plotted in several ways. Marlow,<sup>7</sup> using a method suggested by Igersheimer,<sup>8</sup> was able to trace offshoots from the blind spots. He thought that they were probably nothing more than evidence of fatigue, although he suggested the possibility that they were shadows cast by the retinal vessels. Evans<sup>9</sup> made possible the practical plotting of these vessel shadows. Gradle, in discussing Davis' paper,<sup>6</sup> commented on the wide scope made possible by Evans' method of angioscotometry.<sup>9</sup> Although Duke-Elder<sup>10</sup> attaches less importance to the plotting of angioscotomas than does Evans, we are convinced that with a cooperative subject the method is valuable as well as accurate and simple. Our procedure is as follows:

We observe Evans' technic closely, using a Lloyd stereocampimeter with a black screen. This instrument has the advantage of eliminating accommodative effort, though the test field is still within a short distance of the patient's eye. Monocular fixation is used. Test objects are made by fusing the ends of a fine silver wire into balls, to which a lusterless finish is given by exposure to hydrochloric acid fumes. The diameter of the test objects, as determined by micrometer measurement, varies between 0.35 and 0.75 mm., which subtends an angle on the retina smaller than the retinal vessels. The illumination on the screen is kept constant at 7 foot-candles, and a "daylight" filter is used. The scotomas are plotted by passing the test objects from the seeing into the nonseeing areas, and the vessels are plotted by passing the objects circumferentially around the blind spot at intervals of 2 mm., the shadows of the vessels being outlined as they are encountered. Signaling is done by the patient tapping on the table.

In none of our cases of pseudoneuritis was there any enlargement of the blind spots or angioscotomas. Conversely, we have never examined a case of proved papilledema in which enlargement of the blind spots was absent. The marked contrast between these findings and those in cases of intracranial neoplasm is apparent. It should be strongly emphasized that in the pathologic nerve heads chosen for comparison the papilledema was of low grade and the elevation of the disk was comparable with that found in pseudoneuritis.

6. Davis, L.: The Blind Spots in Patients with Intracranial Tumors, J. A. M. A. **92**:794 (March 9) 1929.

7. Marlow, S. B.: New York State J. Med. **23**:369, 1923.

8. Igersheimer, J.: Arch. f. Ophth. **96**:1, 1918.

9. Evans, J. N.: Am. J. Ophth. **9**:489, 1926; Brit. J. Ophth. **11**:369, 1927.

10. Duke-Elder, W. S.: Text Book of Ophthalmology, London, Henry Himpton, 1932, vol. 1.

Theoretical explanations of the enlarged blind spots which are encountered in papilledema and not in pseudoneuritis, hardly fall within the scope of this paper. A few of the more common conceptions, however, may be mentioned. The first is that the swollen nerve head displaces, to a greater or lesser degree, the rods and cones of the peripapillary area. There is also a peripapillary detachment of the retina in certain of these cases (Reese<sup>11</sup>). Evans<sup>12</sup> referred to the drainage system linking the retinal perivascular lymph spaces with the perineural spaces and the subarachnoid spaces of the optic nerve. Obstruction to this drainage, he believed, causes enlargement of the angioscotomas. The same mechanism operating on minute vessel twigs arising from the vascular circle of Zinn, which nourishes the peripapillary area, may account for the enlargement of the blind spot itself.

#### REPORT OF CASES

##### CASE 1.—*Pseudoneuritis associated with a refractive error.*

*History.*—M. G., a schoolgirl, aged 8, when first seen on Dec. 3, 1932, complained chiefly of headaches, lassitude and irritability, which was particularly noticeable after she returned from school each day. At an examination at the Brooklyn Eye and Ear Infirmary there was a difference of opinion as to whether the appearance of the nerve heads represented pseudoneuritis or papilledema. The patient was taken to Dr. I. Goldstein, who subsequently permitted us to study her.

*Examination.*—In both eyes the nerve heads were reddish; the margins were blurred, the nasal margins more so than the temporal. The arteries were normal in size. The veins were perhaps slightly wider than normal. No hemorrhages or exudates were present. The macula and periphery were normal. In each eye vision was 20/30 and there was a total hyperopia of +3.5 diopters.

Physical and neurologic examination revealed no abnormalities, nor did roentgenograms of the skull, the peripheral visual fields or the blind spots. Glasses were prescribed and these relieved the symptoms. There has been no change in the appearance of the nerve heads.

##### CASE 2.—*Congenital pseudoneuritis.*

*History.*—A. C., a man, aged 32, a painter, was admitted to the Mount Sinai Hospital on April 12, 1929, with a diagnosis of gastric ulcer. He was readmitted on June 26, 1932, to the service of Dr. Kessel, because of recurrence of the pain and of his having one tarry stool. Treatment with a Sippy diet and atropine was followed by the disappearance of symptoms.

*Examination.*—On each admission the findings in the fundi were as follows: In the right eye, the nerve head was reddish. The markings and margins, except the temporal ones, were obscured. In the physiologic cup and on the vessels over it there was a deposit of glial tissue which extended along the vessels for a short distance. The remainder of the fundus was normal. No hemorrhages or exudates were seen. In the left eye, the nerve head had the same appearance as that of the right eye, save that the changes were more marked. Over the physiologic

11. Reese, A. B.: Tr. Am. Ophth. Soc. 28:341, 1930.

12. Evans, J. N.: An Interpretation of Defects in the Visual Field, Arch. Ophth. 3:153 (Feb.) 1930.

cup there was a heavy deposit of glial tissue, which extended well along the vessels. The fundus was otherwise normal.

The blind spots, visual fields and neurologic status were normal, and the refraction, under cycloplegia, was: right eye, +1.75 sphere, equals 20/20; left eye, +1.00 sphere, equals 20/20.

*Diagnosis.*—Principally because of the heavy perivascular sheath of connective tissue extending several disk diameters from the nerve head, the condition was considered congenital.

*CASE 3.—Congenital pseudoneuritis.*

*History.*—J. G., a housewife, aged 48, came to the ophthalmologic clinic in February, 1932, complaining of ocular fatigue and inability to see well at close range. There was also moderate epiphora. The patient had long-standing hyperthyroidism.

*Examination.*—Beyond a refractive error and unusual appearances in the eyegrounds, no abnormalities were found.

The ocular nerve heads were enlarged, red and somewhat elevated. The margins were markedly blurred, and around each nerve head was an indistinct, paler ring, which may have represented a much obscured scleral ring. The vessels as they came off the nerve heads were accompanied by white lines which probably represented a congenital deposit of glial tissue. These extended for a short distance from the nerve head. The vessels presented a striking appearance, as there was an extreme amount of tortuosity of all the branches (fig. 1). The veins were widely dilated. No hemorrhages or exudates were present.

*Course.*—There has been no change in the nerve heads since the patient was first seen. The visual fields and blind spots are normal. The refraction, under cycloplegia was: right eye, -0.25 sphere, -1.00 cylinder, axis 100 degrees, equals 20/30; left eye, -0.25 sphere, -1.00 cylinder, axis 90 degrees, equals 20/30.

*CASE 4.—Pseudopapilledema.*

*History.*—R. O., a housewife, aged 35, was admitted to the service of Dr. B. S. Oppenheimer on Feb. 1, 1932, because of epigastric choking and gagging which had been present for eight years. The symptoms had been increasing for five months prior to admission.

*Examination.*—Physical examination gave negative results. In the right eye, the nerve head was pale, with obliterated markings and margins. The veins showed slight fullness; the arteries were not particularly narrow. Several of the vessels showed perivasculitis on and about the disk. There was moderate peripapillary edema, and the swollen nerve head had a mushroom appearance. The elevation of the disk was 2.5 diopters. There were no hemorrhages or exudates (figs. 3 and 4). In the left eye, the nerve head was pale but still had some pink color. The arteries showed slight narrowing. Some of the vessels showed slight perivasculitis. There was moderate peripapillary edema. The elevation of the disk was 1.5 diopters; there were no hemorrhages or exudates.

*Diagnosis.*—The ophthalmologist considered the condition to be papilledema with postneuritic atrophy. A neurologic consultant, however, made the following statement: "The picture presented by the fundi is far from normal, but it does not impress me as being definitely that observed in increased intracranial pressure or inflammatory disease. The neurologic status is otherwise normal. Further study of the eyegrounds is necessary."

*Course.*—The patient has been observed up to the present time, and no change has occurred in the appearance of the fundi. She has entirely recovered from her complaints. The blind spots and visual fields are normal. The vision in



Fig. 1 (case 3).—Photograph of the fundus in a case of the congenital type of pseudoneuritis.

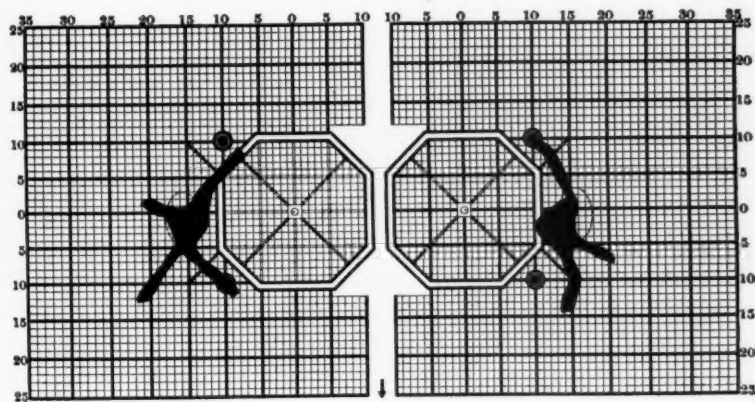


Fig. 2 (case 3).—Blind spots and angioscotomas.



Fig. 3 (case 4).—Photograph of the fundus in a case of pseudopapilledema.

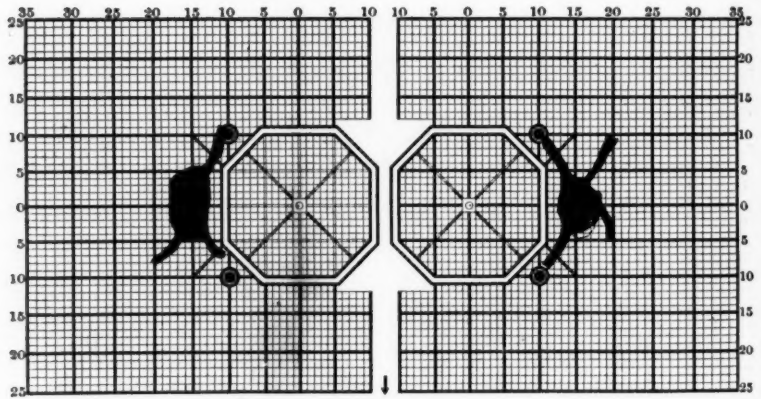


Fig. 4 (case 4).—Blind spots and angioscotomas.

each eye is normal, refraction under cycloplegia being: right eye, +0.75 sphere, equals 20/20; left eye, +0.50 sphere, equals 20/20.

In the absence of any change in the appearance of the nerve heads for over a year, and of any neurologic manifestations, and in view of the fact, which is of most importance, that the blind spots and angioscotomas are normal, we believe this to be a case of pseudopapilledema.

CASE 5.—*Pseudopapilledema.*

*History.*—E. V., a girl, aged 8 years, was admitted to the service of Dr. I. Strauss on June 7, 1930, and was discharged on July 5. There was a history of chronic headaches of a migrainous character for several years prior to admission. The family and past histories were without significance save for whooping cough and measles. Studies conducted in the pediatric and ophthalmologic clinics failed to elicit any positive information, but the appearance of the nerve heads was unusual and caused a considerable amount of controversy.

*Examination.*—The nerve heads were reddish, and the disks were elevated to 1.5 diopters. The margins, while discernible, were indistinct. No edema, exudates or hemorrhages were present. The vessels were normal.

Studies of the visual fields and blind spots gave negative results. The total refractive error under cycloplegia was: right eye, +1.25 sphere, +2.50 cylinder, axis 90 degrees, equals 20/20; left eye, +0.50 sphere, equals 20/20.

*Course.*—The child has been observed in the neurologic follow-up clinic from her discharge until the present time. She still has headache occasionally, but the picture of the fundi is unchanged. No other positive findings have been obtained. Lumbar puncture, encephalography and other neurologic studies have given uniformly negative results.

CASE 6.—*Pseudopapilledema.*

*History.*—N. S., a woman, aged 40, was admitted to the service of Dr. B. S. Oppenheimer on Jan. 13, 1932, for a recent hematemesis. On admission marked anemia was found. During the patient's stay in the hospital, routine examination revealed what appeared to be pathologic nerve heads.

*Examination.*—The report of the ophthalmologist on Jan. 26, 1932, was: In the right eye, the nerve head was reddish, with markings and margins much obscured. There was about 2 diopters of elevation of the disk. In the center of the nerve head there was a deposit of glial tissue, but the physiologic cup could be made out. The arteries were slightly irregular in caliber, and the veins were engorged and tortuous. At the lower pole of the nerve head, at 7 o'clock, there was a hemorrhage into the nerve fiber layer which was absorbing it. The macula and periphery were normal. In the left eye, the appearance of the nerve head was similar to that of the right eye. There was about 1.5 diopters of elevation of the disk. The vessels did not show as much change as in the right eye. The macula and periphery were normal. No hemorrhages were seen.

*Diagnosis.*—The ophthalmologist considered the condition to be bilateral papilledema, although the possibility of pseudoneuritis was entertained. The hemorrhage on the right side was thought to be associated with the low hemoglobin content, which at one time fell to 27 per cent. A diagnosis of a gastro-intestinal neoplasm with intracranial metastases was considered, and the patient was studied from this point of view.

*Course.*—In the fourteen months during which we have followed this patient, there has been no change in the appearance of the fundi other than the resorption of the single hemorrhage seen. The blind spots are normal. Total refraction under cycloplegia was: right eye, +1.25 sphere, equals 20/20; left eye, +1.00 sphere, equals 20/20.



Fig. 5.—Photograph of papilledema of 2 diopters in a case of tumor of the brain proved at operation. (The tumor was a glioma situated in the left temporal lobe.)

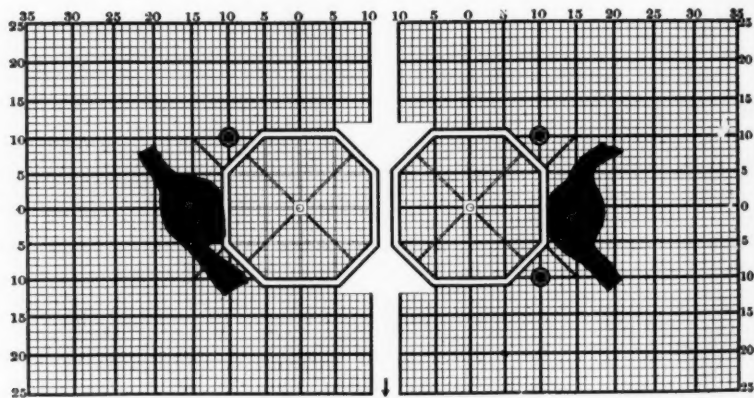


Fig. 6.—Blind spots and angioscotomas in the case shown in figure 5.

## SUMMARY

Cases in which the nerve heads appear to be pathologic but so far as one can determine are not may be divided into three main groups. The first group, in which the appearance of the nerve heads resembles optic neuritis rather than papilledema, is found in the presence of marked refractive errors. This appearance is fairly characteristic. The second group consists of cases which resemble optic neuritis in which there are congenital changes of the nerve heads and vessels, frequently with deposits of glial tissue. In this group the nerve heads have definite morphologic characteristics. The third group is composed of cases in which the appearance of the nerve heads resembles papilledema more than optic neuritis, and presents a difficulty in differential diagnosis. Whether or not the picture in the last group of cases represents a previous pathologic condition we cannot positively state. No definite history to suggest this was obtainable in our cases, nor were there any changes in the visual fields or loss of vision which might have indicated a previous local disease. One patient entered the hospital with severe anemia, and there may have been a relationship between that condition and the appearance of the nerve heads.

For the recognition of these cases of nerve heads of unusual appearance, particularly those of the last group, we believe that there are two criteria of major importance. The first is absence of change of the nerve heads. Followed closely by photographs, the nerve heads in all of our cases have shown absolute permanency up to the present time. As is well known, there is usually some evidence of progression or retrogression of pathologic states from week to week, and certainly from month to month.

The second criterion is the size of the blind spots and angioscotomas. We believe that with accurate plotting under standard conditions the vast majority of pathologic conditions will reveal enlargement and widening of the angioscotomas on the first examination. If the blind spots and angioscotomas are normal on repeated examination, we believe that the appearance of the nerve heads can be safely dismissed as benign.

Observations made with a relatively red-free light (Eastman Wratten 61-N gelatin filter)<sup>13</sup> gave no information of particular value, save that it facilitated the detection of minute hemorrhages in pathologic conditions.

## DISCUSSION

DR. JOHN N. EVANS: It is my belief that this paper has a much greater significance than one is apt to realize at first thought. Besides the indications furnished by swelling of the nerve head, the ophthalmologist has been able to gain

13. Dobson, M. A.: *Am. J. Ophth.* **11**:431, 1928.

some information about the presence of increased intracranial pressure from the study of the pulsations of the retinal vessels through the use of the ophthalmoscope in conjunction with the dynamometer of Bailliart. Recognition of the presence of increased intracranial pressure through the changes in the angioscotomas, as elucidated in the presentation of Drs. Weiss and Lambert, adds a link to the chain of angioscotometry. Angioscotometry as a branch of perimetry was first evolved in 1925, since which time interest in it has been manifested by numerous contributions. When one realizes that the so-called shadows of the vessels may be tremendously widened by certain factors which bear on the problems of increased intracranial pressure, a new interest for the neurologist is disclosed.

The explanation of how the changes in the angioscotomas come about is dependent on evidence drawn from numerous sources; but changes in the system of the retinal perivascular space seem to account for most of the clinical pictures. Satisfactory injections into the perivascular spaces—not only in the eyes of animals, but in normal living human eyes—have been made. There seems to be a distribution of injected prussian blue not only about the vessels but about the ganglion cells and along the axons and into the substance of the retina. A study of the tissues with the binocular microscope localizes the deposited pigment definitely.

DR. THOMAS H. JOHNSON: The experienced observer will not have great difficulty in differentiating the authors' two types of pseudoneuritis from true neuritis.

However, in the cases of pseudopapilledema the problem is not easy. I saw the fundi in case 4, and objectively the appearance of the nerve heads was that of receding papilledema. The thing that is puzzling and that cannot be explained is that the blind spots were normal in these cases. In no case of papilledema in which perimetric studies were made do I recall having seen a blind spot of normal size. On the other hand, I cannot reconcile with a normal nerve head the edema, the elevation, the deposit of connective tissue on the disk and along the arteries and the abnormally narrow arteries described as existing in these cases of pseudopapilledema. In my experience, papilledema in cases of cerebral neoplasm does not remain stationary. In chronic hydrocephalus, however, the pathologic state of the disk may remain unchanged over a period of many years. In a case of slowly growing orbital tumor which I observed for about four years prior to enucleation of the eye with removal of the tumor, papilledema of 2 diopters did not change.

To me, the changes noted in the nerve heads in the cases of papilledema appear to be abnormal, and although they evidently are not due to increase of intracranial pressure, I believe that they are secondary to a pathologic process which may have been active in the remote past. It is no less difficult to explain the obvious abnormalities of the nerve heads in these cases than to explain the presence of normal angioscotomas.

This is a subject of importance and of interest to neurologists and ophthalmologists. It would be instructive if these patients could be kept under observation for several years.

What is the explanation for the disproportion in the size of the angioscotomas and the blind spots, as compared with the relative size of the retinal vessels and the nerve head?

DR. LAWRENCE S. KUBIE: Is the increase of diameter of the vessels great enough to be detected under the magnification obtainable with an ordinary ophthalmoscope, particularly if it is equipped with a measuring grid, such as that on the Keeler ophthalmoscope? It would be useful to form a judgment by direct

observation if this were possible. Second, are both the arteries and the veins enlarged, or is the angioscotoma largely venous, or is there a difference between the arteries and veins? If the enlargement is due to the vessels themselves, one would expect only the veins to be enlarged. If it is an enlargement of the perivascular spaces it would probably not be possible to detect this by ophthalmoscopic observation.

By way of contrast to these cases, which have been under observation for one to two years, I recall a case which several years ago caused controversy in Baltimore. A young woman, who was first seen because of headaches, went to an ophthalmologist who found that she had both definite papilledema of low grade and a low refractive error. He corrected the refractive error, and the headaches disappeared; but the papilledema persisted for three years. During this time she was under the observation of Dr. Dandy. At the end of the three years, during which time there had been no change in the papilledema and no neurologic disturbance of any kind, Dr. Dandy made an injection of air and demonstrated an obstruction in the third ventricle of such a nature that air would fill either lateral ventricle but not the third ventricle. On splitting the corpus callosum he found a small tumor hanging by a shred of ependymal tissue between the foramina of Monro and acting as a ball-valve in the ventricular system. When this tumor was removed the papilledema subsided. During the entire period there had been no diminution in visual acuity. This, then, was an asymptomatic case of low grade papilledema of three years' duration caused by an intracranial tumor. It raises the interesting question of how a tumor of that type can produce papilledema with low grade intermittent pressure.

DR. HERMAN SELINSKY: Dr. Strauss requested me to report a case belonging to this group that he has observed for twenty years. The patient first presented bilateral papilledema and was referred to a neurosurgeon. Exploration was made, and no lesion was found. The patient made an uneventful recovery from the operation; he has had no symptoms subsequently, and the fundi present the same picture now as at the original examination. Does the method of Magitot throw any light on the status of the vessels in the retina in these cases?

DR. R. K. LAMBERT: In answer to Dr. Kubie's first question, we have tried to determine differences in the width of the vessels with the Keeler ophthalmoscope and other forms of retinal measuring grids; while this seems possible theoretically, in our hands it has not been so. The size of the nerve heads and large lesions can be measured by this method.

As to whether the angioscotomas are arterial or venous, the answer to that will throw light on Dr. Johnson's comment that there seems to be a disproportion between the retinal shadows and the blind spots. The angioscotomas represent both arteries and veins. The arteries and veins leave the optic disk together, i. e., in pairs. One cannot differentiate between them, and one gets a shadow of both types of vessels and presumably of the perivascular space at the same time.

In regard to the case mentioned by Dr. Kubie, in which encephalography was used, two of our cases have been studied in this way, but not the others. The two cases belonged to the pseudopapilledema group.

In answer to Dr. Selinsky's question regarding the method of Magitot, I presume he referred to measurement of the blood pressure in the retinal vessels. The method of Bailliart, applied by Magitot, was studied by Berens and his co-workers in 1928. It was found useful in detecting increased intracranial pressure in the absence of papilledema.

DR. HERMAN WEISS: The only thing I can add is to emphasize the fact that the shadows of the vessels, and not the vessels, are plotted in the angioscotomas.

## MYELITIC AND MYELOPATHIC LESIONS

### V. COMPRESSION OF THE SPINAL CORD BY EXPANDING LESIONS PRODUCING MILD, MODERATE OR MARKED INTERFERENCE WITH THE CIRCULATION LEADING TO MYELOPATHY

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AND

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Expanding lesions in or about the spinal canal may compress the spinal cord and impair or destroy its functions by producing within it minimal, moderate or marked interference with the circulation.

#### CASES PRODUCING MILD INTERFERENCE WITH THE CIRCULATION

Expanding lesions that directly compress the spinal cord without producing interference with the circulation are relatively rare. In cases in which very mild interference with the circulation occurs, it plays an insignificant rôle in the causation of the signs and symptoms. In such cases the neurologic manifestations are primarily due to pressure causing disturbances in the conductivity of the fiber tracts. The histopathologic changes are correspondingly very slight.

Six cases of this type were found in our series. For the sake of brevity, only one will be described in detail, and the remaining five will be summarized briefly.

**CASE 1.**—B. D., a man, aged 52, was admitted to the Montefiore Hospital on Aug. 20, 1931. Some months before he had had continuous pain in the mid-thoracic region of the back and paroxysmal pains in the lower extremities. In August, there suddenly appeared numbness and complete paraplegia of both lower extremities with constipation and urinary disturbances.

*Neurologic Examination.*—There were hyperactive tendon reflexes in the upper extremities, with spastic paraplegia and a bilateral Babinski sign, loss of all forms of sensation from the toes to the level of the fifth thoracic segment (more marked on the right) and tenderness over the fourth dorsal spine.

*Laboratory Data.*—The spinal fluid contained 40 cells per cubic millimeter and gave a strongly positive Pandy reaction. Manometric studies revealed no block. Roentgen examination showed collapse of the ninth dorsal vertebra.

*Course.*—Five days after admission, the patient became comatose and paralytic ileus developed, from which he died on the next day.

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From the Neuropathological Laboratory, Montefiore Hospital.

Read at the Fifty-Eighth Annual Meeting of the American Neurological Association, June 7, 1932, at Atlantic City.

*Diagnosis.*—The diagnosis was metastatic neoplasm of the spine with compression of the spinal cord.

*Necropsy.*—Macroscopic Examination: The dura between the fifth and the eighth dorsal segments was markedly thickened, especially anteriorly (fig. 1).

Microscopic Examination: With myelin sheath stains sections of the cord at the sixth dorsal segment presented an extensively thickened dura, which was more marked on the anterior surface, where it was invaded by a tumor (fig. 1). There was little demyelination of the fiber tracts. Under higher power magnification, however, there were seen several small patches of demyelination in the anterior region of the cord. At the eighth dorsal segment the lateral and ventrocerebellar tracts had a honeycombed appearance. In one area the lower border of the posterior column was also demyelinated. Although the tumor was extensive, the anterior and posterior spinal vessels showed little evidence of compression. The walls of the right lateral spinal artery were slightly thickened, and its lumen was nar-



Fig. 1.—Myeloma invading the ventral spinal dura at the fifth and eighth dorsal segments producing a mild myelopathic process. Myelin sheath stain (Weil modification).

rowed. The anterior horn cells disclosed only some retrograde changes consisting of poorly stained Nissl substance. Sections above and below the tumor showed neither ascending nor descending degeneration. The axis cylinders, except those of the lateral corticospinal tract at the eighth dorsal segment, which were swollen, showed no changes (fig. 2). The glial response was normal. The invading tumor was a myeloma.

The microscopic diagnosis was mild myelopathy.

*Comment.*—The rapid onset of the neurologic signs was due probably to a sudden invasion of the spinal dura by the myeloma. In spite of the fulminant invasion, the histopathologic changes in the cord were unusually slight. This was most likely due to the incomplete compression of the spinal vessels.

CASE 2.—B. C., a man, aged 61, was admitted to the hospital with a history of paresthesias of the left hand and forearm, weakness of both lower extremities and frequent micturition for the preceding eighteen months.

Neurologic examination, including manometric studies of the spinal fluid, indicated the presence of an extramedullary neoplasm at the third thoracic segment.

Necropsy disclosed a metastatic (primary in the lung) extradural tumor compressing the upper thoracic region of the cord. The cord was not softened.

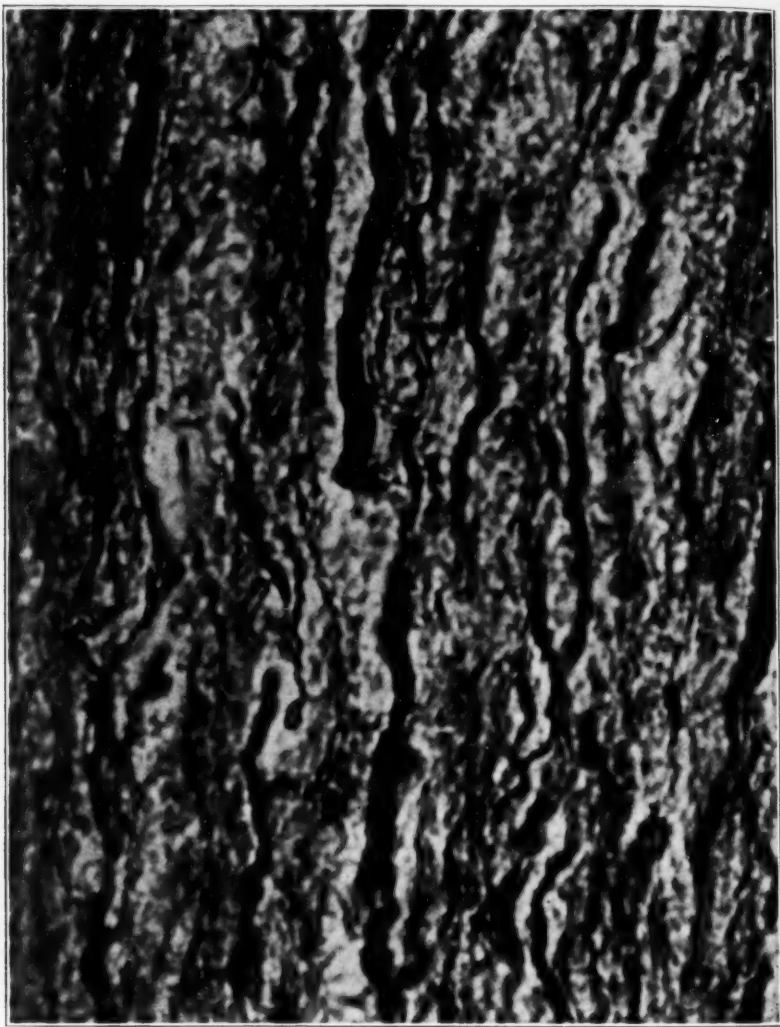


Fig. 2.—Longitudinal section showing swelling of the axis cylinders. Bielschowsky stain;  $\times 440$ .

Histopathologically, slight destruction of the fiber tracts in the compressed area was present. The anterior horn cells were more affected than the white matter. Occasional swelling and fragmentation of the myelin sheaths and axis cylinders with little or no change in the glial elements were observed.

The microscopic diagnosis was mild myelopathy.

CASE 3.—P. S., a woman, aged 51, was admitted to the hospital with a carcinoma of the thyroid gland and generalized metastases. Neurologic examination disclosed evidences of a lesion of the spinal cord due to an extramedullary neoplasm at about the fourth thoracic segment.

At necropsy, extradural metastatic (primary in the thyroid gland) tumor nodules were found at the third and fourth dorsal vertebrae, with distortion of the cord in this region. The histopathologic process resembled that in case 1.

The microscopic diagnosis was mild myelopathy.

CASE 4.—E. L., a woman, aged 54, was admitted to the hospital with carcinoma of the breast and metastases in the lower cervical vertebrae, with neurologic signs of a lesion at the seventh cervical segment of the cord.

Necropsy revealed an extradural metastatic (primary in the breast) tumor opposite the seventh cervical segment, compressing the cord. The myelin sheaths, axis cylinders and glia showed minimal pathologic changes.

The microscopic diagnosis was mild myelopathy.

CASE 5.—D. S., a man, aged 40, was admitted to the hospital with generalized lymphosarcomatosis and neurologic signs pointing to diffuse involvement of the spinal cord.

At necropsy, a continuous sheet of tumor tissue adherent to practically all the vertebrae and dura was found. The histopathologic process in the cord was negligible and resembled that in case 1.

The microscopic diagnosis was mild myelopathy.

CASE 6.—L. F., a woman, aged 52, was admitted to the hospital with symptoms and signs of a neoplasm in the region of the cauda equina.

At necropsy, firm fibrous nodules were found in the cauda equina region, compressing the sacral cord. Microscopic examination revealed an inflammatory process causing arachnoiditis with compression of the roots and lower part of the cord. The changes in the vessels were apparently insufficient to produce interference with the circulation.

The microscopic diagnosis was mild myelopathy.

#### CASES PRODUCING MODERATE OR MARKED INTERFERENCE WITH THE CIRCULATION

Expanding lesions that compress the spinal cord producing moderate or marked interference with the circulation are much more frequent. In these cases the symptoms are due to functional disturbances of the cord from the combined effect of pressure by the expanding lesion on the substance of the cord and interference with the circulation from partial or complete occlusion of blood vessels. The distribution of the pathologic process depends on whether the expanding lesion exerts pressure on the anterior or on the posterior spinal arteries or their branches. The severity of the process, on the other hand, depends on the degree of interference with the circulation. In cases of moderate interference the pathologic process is less severe and the impairment of the functions of the cord slight and gradual in onset. Prolonged moderate compression, unless relieved, may cause complete vascular obstruction and lead to softening. Complete vascular obstruction may

also occur suddenly and rapidly produce signs and symptoms of complete loss of function of the cord at or near the site of compression.

**CASE 7.**—O. C., a man, aged 32, who was admitted to the hospital on Nov. 10, 1930, in 1925 had experienced severe pains in the shoulder blades, radiating over the trunk; this was followed by a girdle sensation at the fifth thoracic segment and paraplegia. A diagnosis of extramedullary tumor of the spinal cord was made, and the patient was operated on three times owing to recurrences. The microscopic diagnosis of the tumor was extradural sarcoma. Later, signs and symptoms developed indicative of metastasis to the lungs.

**Neurologic Examination.**—There were weakness and atrophy of the left forearm and hand, hyperactive tendon reflexes, a bilateral Babinski sign, diminished abdominal reflexes, and hypesthesia, hypalgesia and hypothermesthesia over the third, fourth and fifth dorsal dermatomes on the left.

**Laboratory Data.**—Roentgen examination revealed evidence of pulmonary metastases.

**Course.**—The patient became progressively worse and died on Feb. 12, 1931.

**Diagnosis.**—The diagnosis was extradural sarcoma and mediastinal and pleural metastases.

**Necropsy.**—Gross Examination: The dura over the thoracic and lumbar regions was thickened, and its outer surface was occupied by a tumor. The spinal cord was atrophic in the upper and midthoracic regions, and the veins were engorged.

**Microscopic Examination:** In sections of the upper thoracic region treated with myelin sheath stains the tumor was seen to be situated on the posterolateral surface of the dura, distorting the cord (fig. 3 A). Some white fibers of the posterior and lateral columns were demyelinated. The posterior and lateral spinal arteries were constricted, their walls thickened and their lumens narrowed. The myelin sheaths were disintegrated, and the axis cylinders in the posterolateral columns were swollen and broken down. There was slight gliosis (fig. 4). Myelin sheath preparations from sections of the lumbar region revealed the neoplasm on the ventrolateral surface of the cord, where (fig. 3 B) the growth compressed the cord very slightly. The myelin sheaths, axis cylinders and glia at this level were normal. The tumor was a sarcoma.

The microscopic diagnosis was moderate myelopathy.

**Comment.**—The changes in the upper thoracic region were due to compression of the vessels of the cord, producing a moderate myelopathic process. In the lumbar region the process was one of slight compression, without vascular interference; this explains the negligible changes in this portion of the cord.

**CASE 8.**—A. L. B., a man, aged 54, was admitted to the hospital with a history and objective findings suggestive of an extramedullary neoplasm of the upper cervical segments. On June 24, 1922, exploratory laminectomy revealed an aneurysm of the right vertebral artery.

Necropsy disclosed an aneurysm of the right vertebral artery compressing the lower part of the medulla and upper cervical segments of the cord. Most of the long tracts of the upper cervical region of the cord were demyelinated; the anterior and posterior spinal vessels were compressed and were moderately sclerotic. There was destruction of the myelin sheaths; the axis cylinders were swollen and partly destroyed. There was slight gliosis. The anterior horn cells in the area of compression showed varying degrees of degeneration.

The microscopic diagnosis was moderate myelopathy.

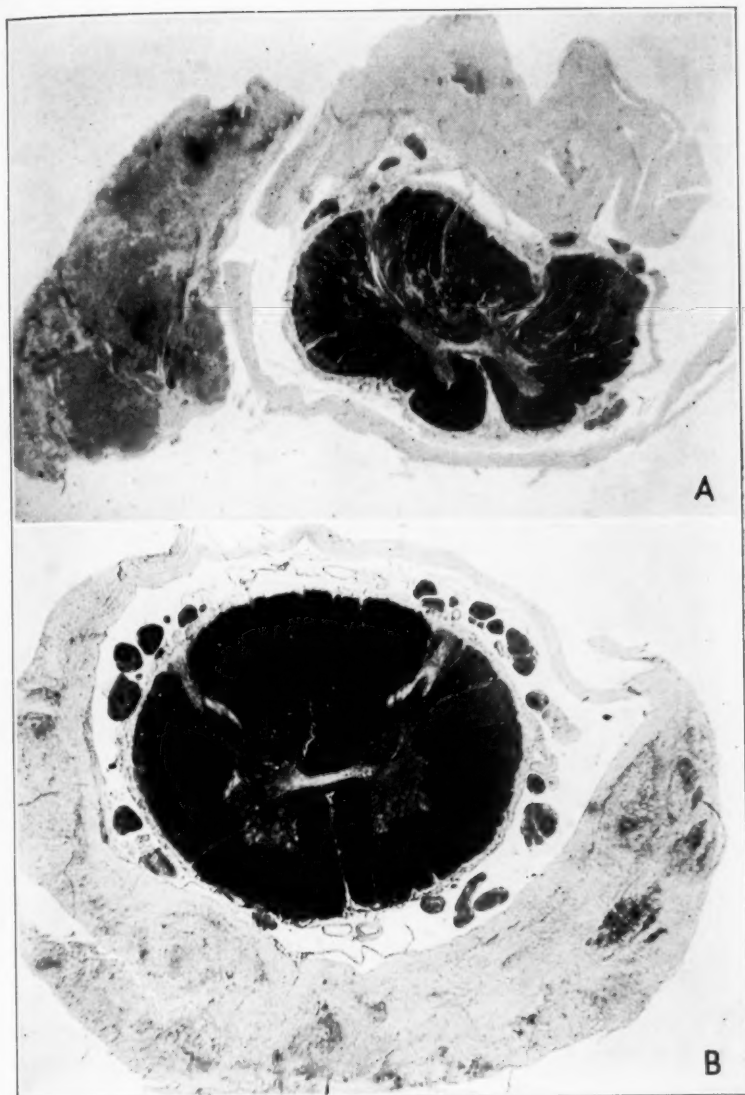


Fig. 3.—*A*, transverse section of the upper thoracic region of the spinal cord showing an extramedullary tumor situated posterolaterally, distortion of the cord and partial demyelination of the posterolateral tracts. *B*, transverse section of the lumbar region showing the ventrolateral portion of the tumor and fair preservation of the spinal cord, except for slight descending demyelination of the left lateral pyramidal tract. Myelin sheath stain (Weil modification).

CASE 9.—I. D., a woman, aged 28, was admitted to the hospital with the clinical picture of an extradural neoplasm at about the second thoracic segment.

At necropsy, an intradural meningioma was found compressing the lower cervical and upper dorsal segments of the cord. The anterior and posterior

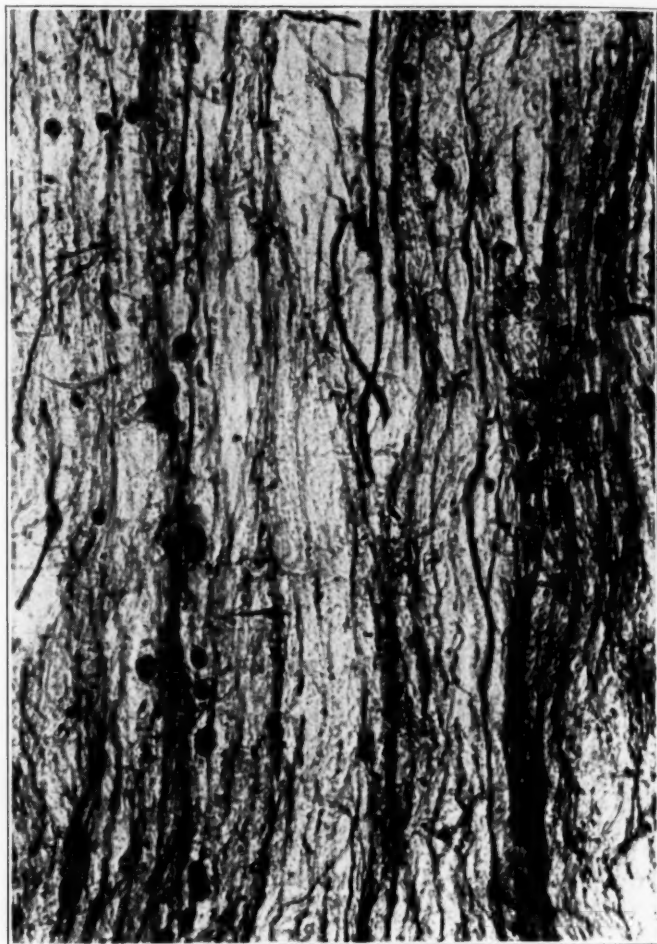


Fig. 4.—Longitudinal section showing slight gliosis in the area of compression. Victoria blue stain;  $\times 440$ .

vessels were compressed. The myelin sheaths, axis cylinders, glia and anterior horn cells showed changes similar to those in case 7.

CASE 10.—R. I., a man, aged 64, had signs and symptoms of an expanding lesion in the region of the lumbar segments of the cord and cauda equina.

At necropsy, a chordoma was found compressing the lower lumbosacral segments. It also compressed the vessels, and the detailed histopathologic changes in the area of vascular compression corresponded to those in cases 7, 8 and 9.

The microscopic diagnosis was moderate myelopathy.

CASE 11.—A. C., a woman, aged 34, was admitted to the hospital with Hodgkin's disease and neurologic signs and symptoms of metastasis to the cord at about the second thoracic segment; one observer considered the possibility of subacute combined degeneration.

At necropsy, small fatty deposits were found scattered throughout the dura. The masses were more extensive between the second and third thoracic segments, where they compressed the vessels of the cord. Sections from the second and third dorsal segments showed partial demyelination of practically all columns of the spinal cord. The more detailed histopathologic changes conformed to those in case 7.

The microscopic diagnosis was moderate myelopathy.

CASE 12.—P. R., a woman, aged 42, was admitted to the hospital with neurologic signs and symptoms of an extramedullary compressing lesion at the third thoracic segment. Laminectomy revealed an extradural meningioma compressing the third, fourth and fifth thoracic segments of the cord. The growth was removed.

At necropsy, the cord appeared constricted and softened at the fifth thoracic segment. The posterior and lateral spinal arteries showed evidences of compression. There was demyelination of the posterior and lateral columns. The changes in the myelin sheaths, axis cylinders and glia were similar to those in cases 7, 8, 9, 10 and 11.

The microscopic diagnosis was moderate myelopathy.

CASE 13.—M. R., a woman, aged 52, was admitted to the hospital in 1928, with the history that in 1917 she had had a meningioma removed from the cord at the ninth and tenth thoracic segments. She remained well until 1927, when the signs of compression of the cord recurred. Two years later, she was again subjected to laminectomy. This time some dural adhesions were found, but no tumor.

At necropsy, the dura was found to be thickened in the lumbosacral region. The blood vessels of the posterior and lateral columns were thickened and had narrow lumens. There was demyelination of the posterior columns and of part of the lateral pyramidal and ventrocerbellar tracts of the lower dorsal and lumbar segments. The myelin sheaths, axis cylinders, glia and anterior horn cells disclosed changes resembling those in case 7.

The microscopic diagnosis was moderate myelopathy.

CASE 14.—M. H., a woman, aged 61, was admitted to the hospital with generalized lymphosarcomatosis and neurologic signs and symptoms of compression of the lower thoracic segments.

At necropsy, the entire chain of lymph glands along the vertebral column was found to be enlarged. There was a thickened dura, with a flat, friable mass limited to the posterior surface of the lower thoracic and upper lumbar segments. Sections of the lower thoracic segments showed demyelination of the posterior columns and crossed pyramidal tracts. The posterior spinal vessels were compressed and thickened and had narrow lumens. The myelin sheaths, axis cylinders and glia revealed changes similar to those in cases 7 to 13 inclusive.

The microscopic diagnosis was moderate myelopathy.

CASE 15.—J. K., a man, aged 32, was admitted to the hospital with physical signs suggestive of a neoplasm in the right side of the chest and neurologic signs and symptoms of subacute combined degeneration of the cord.

At necropsy, numerous extradural lymphoid masses were found in the posterior portion of the cord at various levels, mainly, in the upper thoracic region. The

posterior spinal arteries were compressed and showed moderate thickening of the walls with narrowed lumens. The degeneration of the fiber tracts was essentially limited to those of the posterior columns and posterior roots, not unlike that observed in *tabes dorsalis*. The changes in the myelin sheaths, axis cylinders and glia were similar to those in case 7.

The microscopic diagnosis was moderate myelopathy.

CASE 16.—H. J., a youth, aged 17, was admitted to the hospital with a diagnosis of lymphosarcoma and with neural signs pointing to compression at the lower thoracic segments of the cord.

At necropsy, fatty tumor-like masses infiltrating the dura and lower thoracic and lumbar regions were found. The cord was softened anteriorly. The posterior and anterior spinal arteries were compressed. There was partial demyelination of the posterior cerebellar and anterior pyramidal tracts in the lumbar segments. The myelin sheaths and axis cylinders in this region were disintegrated; there was slight gliosis.

The microscopic diagnosis was moderate myelopathy.

CASE 17.—F. H., a woman, aged 80, was admitted to the hospital with a history of weakness in the lower extremities and neurologic symptoms and signs of an expanding lesion at the midthoracic segments.

At necropsy, there were extensive thickening of the dura (meningioma) and adherence of the pia-arachnoid in the middle and lower dorsal regions to the spinal cord. The cord in this region appeared thin and soft. The posterior and especially the anterior spinal arteries were compressed. There was flattening of the cord between the seventh and the tenth dorsal segments with demyelination of the posterior and lateral pyramidal tracts. The myelin sheaths, axis cylinders and glia showed the same pathologic changes as in case 7. In spite of the patient's age (80 years), the atherosclerotic changes in the vessels of the cord were surprisingly slight.

The microscopic diagnosis was moderate myelopathy.

#### CASES PRODUCING MARKED INTERFERENCE WITH CIRCULATION

CASE 18.—H. S., a man, aged 36, was admitted to the hospital on Sept. 29, 1921, with the history that three years before he had begun to have pains in the stomach and a drawing sensation in the knees radiating to the thighs and hips. He also experienced sensations of "freezing" and "pins and needles" in the left foot, which soon extended to the right foot. Gradually there appeared weakness and stiffness in both lower extremities and difficulty in walking. Following lumbar puncture, paraplegia with sphincteric disturbances set in.

Neurologic examination on admission revealed evidences of an extramedullary compressing lesion between the fifth and the twelfth dorsal segments, and on November 26, he was subjected to a laminectomy. On removing the fourth, fifth, sixth, seventh and eighth dorsal laminae, an extradural tumor was found surrounding the entire dural sac, more on the left and posteriorly. The tumor could not be completely extirpated. Following operation the symptoms of disturbance of the cord became more marked. A pleural effusion developed suggestive of an intrathoracic neoplasm. Death occurred on March 13, 1923.

The diagnosis was extradural sarcoma with extension to the adjacent tissues and metastases to the liver, spleen, retroperitoneal and mesenteric lymph nodes, hydrothorax (right), and atelectasis of the right lung.

*Necropsy.*—Gross Examination: The cord was soft, mushy and flattened in the lower dorsal and lumbar regions. In the upper dorsal region there were

several small, discrete, granular, grayish masses, mostly on the right side, attached to the dura. Beginning at the lower dorsal region and extending downward the dura was thick and firm, measuring in the lumbar region from 3 to 4 mm. Sections from the cord and cauda equina showed no direct invasion by the tumor.

**Microscopic Examination:** Sections of the lower dorsal and lumbar regions showed with the myelin sheath stain an extradural tumor with distortion of the cord and almost complete demyelination of all fiber tracts (fig. 5). In sections stained with sudan IV, the cord was seen to be filled with compound granular corpuscles. With the hematoxylin-eosin and Mallory stains the meninges were thickened, and the normal architecture of the cord was completely destroyed. The gray and white matter were equally affected, and the anterior horn cells showed



Fig. 5.—Various segments of the spinal cord showing compression, distortion and destruction of the cord by the extradural neoplasm. Myelin sheath stain (Weil modification).

various degrees of degeneration, some being completely destroyed. The lesion in the lumbar region was more marked than that in the lower dorsal region. The blood vessels in the meninges and cord showed signs of obstruction (thickened walls and narrowed lumens). Longitudinal sections stained by the myelin sheath method showed in the area of destruction complete disintegration of the myelin sheaths (fig. 6). With the Bielschowsky stain, some axis cylinders appeared broken down; others had a corkscrew appearance; still others were completely destroyed (fig. 7). With the victoria blue stain, the cord had a honeycombed appearance and there was a poor glial response (fig. 8).

The microscopic diagnosis was marked myelopathy.

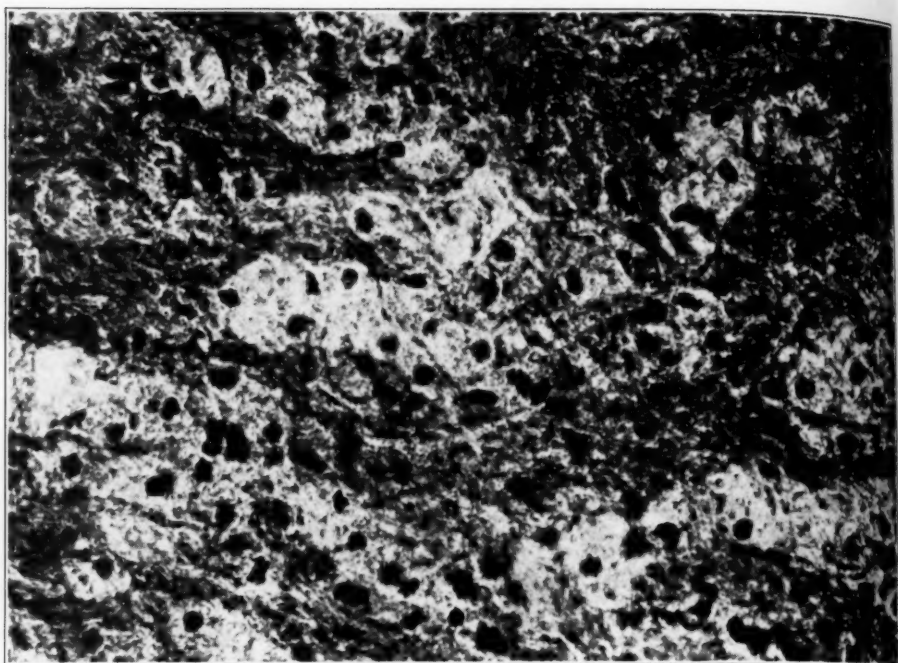


Fig. 6.—Longitudinal section showing destruction of the myelin sheaths. Myelin sheath stain (Weil modification);  $\times 440$ .



Fig. 7.—Longitudinal section showing destruction and breaking down of axis cylinders. Bielschowsky stain;  $\times 440$ .

*Comment.*—The extradural sarcoma caused a marked myelopathic process. The myelin sheaths and axis cylinders showed more extensive changes than were shown in the cases of moderate myelopathy, and there was poor glial response. With such extensive changes, restoration of the function of the cord could not be expected even if the tumor had been completely extirpated.

CASE 19.—I. B., a boy, aged 14, was admitted to the hospital with the history of gradually increasing weakness of all four extremities for two years. Neurologic examination revealed motor and sensory signs referable to a lesion of the upper cervical segments of the cord, which was variously interpreted as due to an atypical Friedreich's ataxia, to subacute combined degeneration, to central

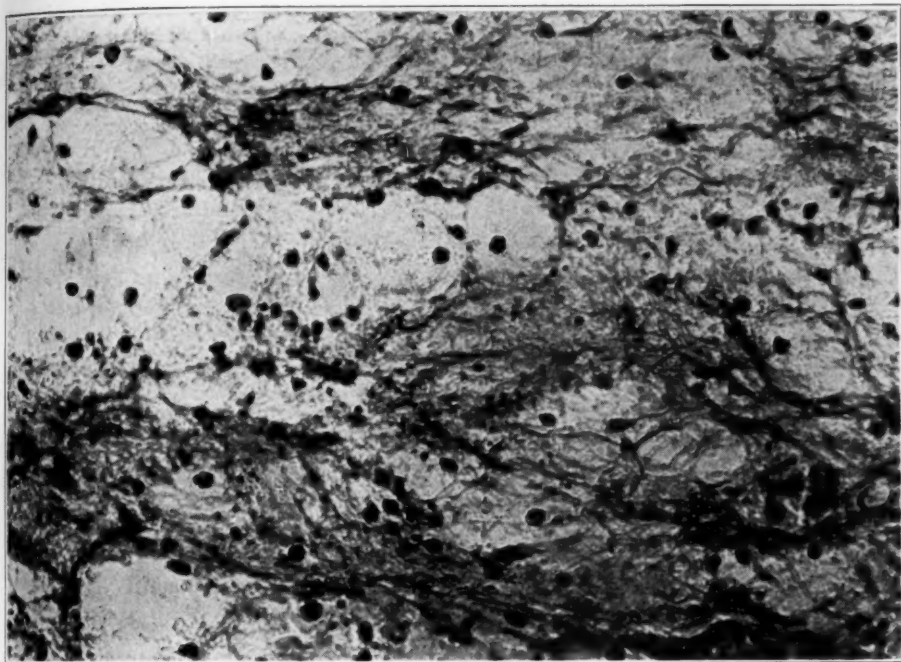


Fig. 8.—Longitudinal section showing poor glial response and honeycomb appearance. Victoria blue stain;  $\times 440$ .

gliosis or to an extramedullary tumor. The condition became progressively worse; in January, 1921, bulbar signs developed, and the patient died on April 5.

At necropsy, an osteofibroma arising from the odontoid process of the second cervical vertebra causing compression of the upper cervical segments of the cord was found. The cord was soft and flattened in the region of the compression. At the level of the tumor (fourth to fifth cervical segments) the cord appeared distorted and showed demyelination, which was more marked in the lateral and anterior columns than in the posterior. The anterior spinal vessels and others also were compressed and had thickened walls with slight narrowing of the lumens. The anterior horn cells, myelin sheaths, axis cylinders and glia showed changes similar to those in case 18.

The microscopic diagnosis was marked myelopathy.

*Comment.*—This case is also one of marked myelopathy and illustrates that an extramedullary tumor compressing the vessels of the cord may produce signs of an intramedullary lesion.

CASE 20.—E. H., a man, aged 40, was admitted to the hospital with signs and symptoms pointing either to a neoplasm of the cord or to subacute combined degeneration.

At necropsy there was disclosed a retroperitoneal lymphosarcoma with metastasis to the lumbar region. There was a spongy fatlike formation on the posterolateral surface of the dura, compressing the spinal cord. At the twelfth thoracic segment the cord showed demyelination of all fiber tracts except the direct pyramidal tracts, which were less affected. The vessels were compressed but did not have narrow lumens. The anterior horn cells showed mild degenerative changes. The myelin sheaths, axis cylinders and glia presented changes similar to those in case 18.

*Comment.*—It is difficult to explain the extensive pathologic changes in the spinal cord in spite of the fact that the vessels in the involved area had no narrow lumens. The prolonged compression (eight years) may have been a factor.

The microscopic diagnosis was marked myelopathy.

CASE 21.—K. J., a man, aged 60, was admitted to the hospital on June 22, 1931, with signs and symptoms of a lesion at the level of the sixth thoracic segment. Laminectomy was performed on July 7, but no neoplasm was found.

At necropsy, a meningioma was found on the dorsolateral surface of the inner part of the dura, compressing the cord at the fifth dorsal segment. At this level the cord was markedly distorted, most of its fiber tracts being completely demyelinated. The posterolateral arteries at the middorsal segments were compressed. The anterior horn cells showed severe cell changes. The histologic appearance of the myelin sheaths, axis cylinders and glia resembled that in cases 18, 19 and 20.

*Comment.*—This is another example of compression of the vessels of the spinal cord by an extramedullary tumor (meningioma) inducing a marked myelopathic process.

CASE 22.—E. J., aged 59, a salesman, suffering from extensive Paget's disease, was admitted to the hospital with symptoms and signs pointing to involvement of several thoracic vertebrae and compression of the spinal cord.

At necropsy, the dura over the lower cervical and upper thoracic regions of the spinal cord was found to be thickened and adherent to the destroyed vertebrae and to the posterior surface of the cord; similar thickenings were observed in the middle and lower thoracic regions. The fiber tracts of the spinal cord in the lower cervical and middle and lower thoracic regions appeared discolored. In sections treated with myelin sheath stains the lower cervical and thoracic segments of the cord appeared distorted, and practically all the fiber tracts were demyelinated. The anterior and posterior spinal arteries were slightly thickened and compressed. The posterolateral vessels were more compressed than the anterior. The anterior horn cells showed various retrograde changes. In longitudinal sections, the changes in the myelin sheaths, axis cylinders and glia resembled those in the other cases of marked myelopathy that comprised the group.

The microscopic diagnosis was marked myelopathy.

## COMMENT

Twenty-two cases are reported in this series, six of mild, eleven of moderate and five of marked myelopathy due to compression of the spinal cord.

In five of the six cases of mild myelopathy, the compression of the cord was due to a metastatic neoplasm, and in one, to arachnitis. The neurologic symptoms and signs were those of a mild compression of the cord. The histopathologic process was somewhat similar in all. The fiber tracts showed hardly any demyelination, and there were slight swelling and destruction of the myelin sheaths as well as some swelling of the axis cylinders which could be seen only under a high power magnification. The changes in the glia were slight and resembled an isomorphous gliosis. In case 1 there were some changes in the anterior horn cells. The blood vessels appeared normal, except in the case of arachnitis, in which they showed moderate thickening. The interference with the circulation in the cord was negligible in cases 1, 2, 3, 4 and 5 and absent in case 6.

In the sixteen cases of moderate and of marked myelopathy, eleven of moderate and five of marked changes, it is noteworthy that the onset of the neurologic signs and symptoms was gradual. This is not surprising in view of the fact that in only one case of the entire group had complete obliteration of a spinal vessel occurred. One would hardly expect a sudden onset unless there had occurred a sudden occlusion of one of the vessels. It can be safely stated that in extramedullary compression of the cord an abrupt increase of symptoms which bears no temporal relation to a previously performed lumbar puncture may indicate a sudden interference with the circulation in the cord from sudden occlusion of a blood vessel. Following removal of an extramedullary compression, restoration of function of the cord is to a great extent affected by the severity of any coexisting myelopathic process that may have been produced by the compressing agent. Obviously, the ideal time to relieve compression of the cord is before the latter has produced myelopathic changes by interference with the circulation.

Four cases (11, 15, 19 and 20) offered considerable difficulties in diagnosis. They were thought to be cases of subacute combined degeneration; this was due probably to the severe secondary anemia which was presented. One of us (Davison<sup>1</sup>) has already emphasized that severe secondary anemia rarely produces subacute combined degeneration of the cord, and that changes in the cord in the presence of a new growth elsewhere in the body should be considered as due to metastases in the vertebrae or in the cord producing interference with the circulation and not to the anemia.

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1. Weil, A., and Davison, C.: Changes in the Spinal Cord in Anemia, *Arch. Neurol. & Psychiat.* **22**:967 (Nov.) 1929.

The posterior and lateral spinal arteries were compressed in five cases (7, 10, 12, 13 and 21), the anterior and posterior in four (8, 9, 16 and 17), all vessels in five (11, 18, 19, 20 and 22) and the posterior vessels alone in two (14 and 15).

The expanding lesions that compressed the vessels of the spinal cord produced histopathologic changes somewhat similar to those produced by thrombosis of the spinal vessels from other causes. In cases in which the interference with the circulation was moderate, the demyelination and destruction of the axis cylinders was not so complete as in the cases in which such interference was marked. There was a slight attempt at glial repair in the former cases and a poor glial response in the latter. In cases in which the interference with the circulation was marked, except in case 20, there were also pronounced changes in the anterior horn cells.

#### SUMMARY

1. Twenty-two cases of expanding lesions within the spinal canal producing interference with the circulation in the cord are described; in six the myelopathic changes were mild, in eleven moderate, and in five marked. The lesions that produced moderate or marked interference with the circulation caused myelopathy much more frequently.

2. The clinical picture in these cases was characterized by a combination of signs and symptoms at the site of compression (root phenomena, muscular atrophies, etc.) with symptoms and signs referable to the myelopathic process in the same segments and to a lesser extent to changes in some of the segments immediately above and below the level of compression.

3. In the cases producing mild myelopathy the histopathologic process consisted of slight swelling of the myelin sheaths and axis cylinders without alterations in the anterior horn cells (except in case 1) and glia. In those producing moderate myelopathy there was destruction of the myelin sheaths and axis cylinders, but it was less severe than in the cases producing marked myelopathy. There was a slight attempt at glial repair in the former and a poor glial response in the latter. The changes in the anterior horn cells were slight in the cases producing moderate myelopathy and severe in those in which myelopathy was marked.

## Clinical Notes

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### ANEURYSM OF THE INTERNAL CAROTID ARTERY

#### Report of a Case Simulating Tumor of the Pituitary

ROBERT ZOLLINGER, M.D., AND ELLIOTT C. CUTLER, M.D., BOSTON

The clinical syndrome produced by an aneurysm at, or near, the junction of the internal carotid artery with the circle of Willis has recently been emphasized by Albright.<sup>1</sup> He reviewed the thirty reported cases of aneurysm in this region and added two new cases.

Albright separated the cases into five etiologic groups. The most common etiologic factor was a congenital defect in the wall of the cerebral vessels. Next in order of frequency were atheromatous changes in the vessels, syphilis, post-traumatic aneurysms, resulting from fractures at the base of the skull, and mycotic aneurysms from infected emboli. He divided the symptoms into two groups: those due to involvement of the adjacent structures and those arising from leakage of blood from the aneurysm into the subarachnoid space. The most common symptoms were internal and external paralysis of the third nerve and involvement of the first branch of the fifth nerve. The third nerve was involved in all of the thirty-two cases. Roentgenograms in two of the cases had shown some destruction of the sella turcica.

Lodge, Walker and Stewart,<sup>2</sup> in 1927, reported a case of a large aneurysm of the left internal carotid in which a clinical diagnosis of a cyst of the pituitary had been made. Roentgenograms had shown absorption of the posterior clinoid processes. Albi,<sup>3</sup> in 1929, reported a case of aneurysm of the left internal carotid artery which in roentgenograms resembled a tumor of the pituitary. The limits of the aneurysm in his case were defined by calcification within its walls.

Aneurysms occurring at, or near, the junction of the internal carotid artery with the circle of Willis must be considered in the differential diagnosis in cases in which the roentgenograms show destruction or erosion of the sella turcica. For this reason we report a case of a large aneurysm of the right internal carotid artery in which the deformity of the sella turcica as shown in roentgenograms was suggestive of a tumor of the pituitary.

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From the Department of Surgery, the Lakeside Hospital, Cleveland.

1. Albright, F.: Syndrome Produced by Aneurysm at or Near the Junction of Internal Carotid Artery and Circle of Willis, *Bull. Johns Hopkins Hosp.* **44**:215, 1929.

2. Lodge, S. D.; Walker, G. F., and Stewart, M. J.: Aneurysm of Left Internal Carotid Artery Simulating Pituitary Tumor, *Brit. M. J.* **2**:1179 (Dec. 24) 1927.

3. Albi, H.: Aneurysma der Carotis interna, einen Hypophysentumor vortäuschend: Ein Beitrag zur Diagnose intrakranieller Aneurysmen, *Fortschr. a. d. Geb. d. Röntgenstrahlen* **39**:890, 1929.

## REPORT OF CASE

*History.*—An unmarried white man, a railroad foreman, 25 years of age, entered the Lakeside Hospital on Dec. 5, 1930, complaining of blindness of the right eye and failing vision of the left eye. Eight years before admission he had received a blow to the right eye during a basketball game. The eye was swollen shut for a month following the injury and it remained "blood-shot" and irritated for six years. Vision gradually decreased in this eye until, two years before admission to the Lakeside Hospital, blurring of vision occurred. He had about twelve attacks of severe right-sided headache at intervals of from three to four weeks. This severe pain always started in the right eye and spread gradually into the right temporal region. When the pain reached this point, the patient became nauseated and at times vomited. After these attacks, vision in the right eye was always decreased.

In 1924, when the patient was 19 years of age, an internal squint of the right eye developed. Two years later, he consulted a physician because of failing vision and the right internal squint. At that time there was slight protrusion of the right eyeball. Vision was not improved by glasses. He was operated on in June, 1930, after a diagnosis of tumor of the right eye had been made. The retrobulbar space was examined through a lateral incision. Following the operation he was blind in the right eye, and within two weeks he noticed a blind spot, shaped like a maple leaf, in the left eye. The side of the face, roof of the mouth, gums and teeth on the right, as far as the midline, seemed numb, but they slowly improved. Soon the right eye retracted deep into the orbit.

When he was admitted to the hospital, vision in the left eye was so poor that he could read the headlines of a newspaper only with difficulty. He complained of a constant buzzing in the right ear and occasional periods of buzzing in the left ear. He felt that he had become more dull mentally and that his general vigor was impaired. There had never been constitutional symptoms suggestive of a lesion of the pituitary. The family history was without significance.

*Examination.*—The patient was well developed, well nourished and intelligent. The physical findings of importance were limited to the head. The head was drawn slightly to the left, and there was some weakness of the right side of the face. There was a scar from the retrobulbar exploration on the temporal side of the right orbit. There was slight ptosis of the right eyelid, with moderate right exophthalmos. The movements of the right eye were sluggish, with evidence of paralysis of the right sixth nerve. The pupil was small and fixed. There was a primary optic atrophy of the right fundus, with an area of old choroiditis below the disk. The arteries in the fundus were contracted.

The pupil of the left eye reacted to light and in accommodation. The ocular movements were normal, but he could read large newspaper print only with difficulty. At times a nystagmus was present, but no exophthalmos. The disk was oval and hyperemic, and the cup very shallow. The veins appeared slightly pale, but the arteries were normal. The limits of the form field in the left eye were normal, but there was a slight scotoma for colors just below and to the temporal side of fixation. The patient frequently saw in connection with this a green-colored image similar in outline to a maple leaf.

Besides the paralysis of the right sixth nerve, there was numbness of the right side of the face down to the lower lip, with a decreased corneal reflex on that side. There was some involvement of the right seventh nerve as shown by a slight weakness of the nasolabial fold on that side. The reflexes of the extremities were hyperactive.

*Laboratory Data.*—The results of blood studies were within normal limits: white cell count, 7,400; red cell count, 3,830,000; hemoglobin, 98 per cent; polymorphonuclears, 52 per cent, and lymphocytes 45 per cent. The Wassermann reaction of the blood was negative.

Roentgenograms of the skull showed a large sella with depression of the floor (fig. 1). The anterior clinoids were pointed, and the posterior clinoids were destroyed. Over the clivus there were several dense linear shadows. These observations, combined with the results of the physical examination, suggested the diagnosis



Fig. 1.—Large sella with destruction of the posterior clinoids. Note the dense linear shadows above the clivus.

of a suprasellar cyst. However, it was difficult to explain how such a lesion could have produced the exophthalmos with destruction of the right optic nerve and no change in the form field of the left eye.

*Operation.*—The right optic foramen was exposed by a right transfrontal approach on Dec. 15, 1930. The foramen was greatly enlarged, with some destruction of the upper flap of the orbit. A large pulsating soft-walled tumor mass extended from the optic foramen on the right apparently into the orbit and backward under the chiasm and down into the right temporal fossa. The left optic nerve and the chiasm up to the emergence of the right optic nerve were normal in appearance. The nerve on the right, from the chiasm forward, was

greatly elongated and pale gray. The right optic nerve was resected to give better exposure. The strong pulsation of the tumor mass was so suggestive of an aneurysm that needling was not attempted and the wound was closed. The course was gradually downward, and the patient died on the day following operation.



Fig. 2.—Drawing made at postmortem examination showing the location of the aneurysm in relation to the chiasm and the base of the skull. The small illustrations are diagrammatic transparencies of the relation of the aneurysm to the sella turcica, the optic chiasm and its vascular origin.

*Postmortem Examination* (limited to the head).—This was done by Dr. Francis Bayless. The subarachnoid fluid was sanguineous, but the leptomeninges over the superior and lateral surfaces of the hemispheres showed no pathologic change. There were several small lacerations of the leptomeninges and cortex on the

anterior and inferior surfaces of the right frontal lobe. The right hemisphere was edematous, and the convolutions were flattened, particularly in its anterior portion.

When the brain was removed, an aneurysm of the right internal carotid artery was exposed; it extended from the foramen to the origin of the middle cerebral artery (fig. 2). The wall of the aneurysm was thick, fibrous and densely adherent to the sphenoid and temporal bones, both of which were deeply eroded, with subsequent asymmetry of the anterior and middle fossae of the skull on the right side. Most of the aneurysmal tract, which measured about 3.5 cm. in its greatest diameter, was situated in the middle fossa, with infringement on the sella turcica by erosion of the right posterior clinoid process and the right lateral side of the body of the sphenoid bone.

The optic chiasm was elevated and displaced to the left. The trochlear nerve crossed the superior surface of the aneurysm and it, as well as the trigeminal, was densely adherent to the wall of the sac; the peripheral fibers of both nerves were lost. The other cranial nerves in this region were displaced but apparently were not involved in the sac. There was a deep concave defect in the right frontal lobe marking the site of the aneurysm. The pituitary was not grossly identified and was apparently incorporated in the fibrous connective tissue forming the medial wall of the aneurysm.

There was evidence of old and recent hemorrhage around the aneurysm, with considerable dark brown pigmentation of the surrounding connective tissue.

On section, only the center of the sac was found to be patent, the major portion of the cavity being filled by a well organized, lamellated blood clot. The internal carotid artery proximal to the sac was dilated and measured 12 mm. in circumference. Distal to the sac the vessels showed no pathologic change. Other cerebral vessels were the seat of mild intimal sclerosis.

*Histologic Examination.*—A section of the medial wall of the sac included the pituitary, which was compressed, flattened and surrounded by dense fibrous connective tissue. The lining of the sac was covered by a depigmented, well organized thrombus, but the wall was dense and fibrous without recognizable medial components. In the connective tissue comprising the outer surface of the sac were many hemosiderin-containing phagocytes.

Several other sections, including the wall of the aneurysm and the adjacent proximal segment of the internal carotid artery, showed medial disruption by vascularized fan-shaped scars, with interruption of elastic fibers. The vasa of the adventitia were the seat of an obliterating endarteritis and showed perivascular lymphocytic infiltration. This perivascular infiltration of lymphocytes and fibrin cells was also seen in the region of medial scarring.

A section of the basilar artery showed a mild degree of intimal sclerosis. Other sections of the brain and meninges showed no pathologic change.

The pathologic diagnosis was syphilitic arteritis, with an intracranial aneurysm of the right internal carotid artery.

#### CONCLUSION

Aneurysms occurring at, or near, the junction of the internal carotid artery with the circle of Willis may produce changes of the sella turcica which in roentgenograms are suggestive of a tumor of the pituitary. A case is reported of a large aneurysm of the right internal carotid artery which simulated a tumor of the pituitary in roentgenograms.

## SPHENO-OCCIPITAL CHORDOMA

### Report of a Case

MEYER CANTOR, M.D., AND LOUIS D. STERN, M.D., DETROIT

The earliest description of chordoma, with recognition of its notochordal origin, was that of Müller<sup>1</sup> in 1858. Luschka,<sup>2</sup> in 1856, and Virchow,<sup>3</sup> in 1857, described identical tumors but failed to recognize a relation to the chorda dorsalis. Because of the fact that these nodules were always found adjacent to cartilage in a stereotyped relation to it, and because they were often associated with an exostosis and gave the microscopic appearance of cartilage cells, Virchow considered them as degenerated cartilaginous tissue. He called them "ecchondrosis physaliphora spheeno-occipitalis." So far-reaching was the influence of Virchow on the medical thought of that time that the work of Müller was ignored, and it was not until the conclusive work of Ribbert and Steiner<sup>4</sup> in 1894 that this erroneous belief was corrected. These authors showed that in the soft tumors of the clivus blumenbachii there was no transition from cartilage to the jelly-like masses of tissue, and that the cartilage and this mucinous tissue lay next to but independent of each other. They further showed that the pathognomonic physaliphorous cells were remnants of the chorda dorsalis. At about the same time Ribbert<sup>5</sup> demonstrated experimentally the derivation of chordoma from the notochordal remnants (nuclei pulposi) in the center of the cartilaginous intervertebral disks, producing tumors of identical gross and microscopic appearance. Following Virchow's publication in 1857, Hasse<sup>6</sup> and Zenker<sup>7</sup> also described cases of ecchondrosis physaliphora. These men, however, were interested in the cases only from the pathologist's point of view. The tumors were accidental findings during autopsy and gave rise to no symptoms.

The first reported case manifesting symptoms was that of Klebs,<sup>8</sup> in 1864; he described a patient who died after a series of tetanic convulsions. At autopsy a cherry-sized tumor was found obliterating the basilar artery. The

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1. Müller, H.: Ueber das Vorkommen von Resten der Chorda dorsalis bei Menschen nach der Geburt und über ihr Verhältnis zu den Gallertgeschwülsten am Clivus, *Ztschr. f. rat. Med.* **2**:202, 1858.

2. Luschka, H.: Die Altersveränderungen der Zwischenwirbelknorpel, *Virchows Arch. f. path. Anat.* **9**:311, 1856.

3. Virchow, R.: Untersuchungen über die Entwicklung des Schädelsgrundes, *Virchows Arch. f. path. Anat.* **11**:33, 1857.

4. Ribbert, H., and Steiner, H.: Ueber die Ecchondrosis physaliphora spheeno-occipitalis, *Centralbl. f. allg. Path. u. path. Anat.* **5**:457, 1894.

5. Ribbert, H.: Ueber die experimentelle Erzeugung einer Ecchondrosis physaliphora, *Verhandl. d. Cong. f. inn. Med.* **13**:455, 1895.

6. Hasse: Ein neuer Fall von Schleimgeschwülsten am Clivus, *Virchows Arch. f. path. Anat.* **11**:395, 1857.

7. Zenker, F. A.: Ueber die Gallertgeschwülste des Clivus Blumenbachii, *Virchows Arch. f. path. Anat.* **12**:108, 1857.

8. Klebs, E.: Ein Fall von Ecchondrosis spheeno-occipitalis amyloacea, *Virchows Arch. f. path. Anat.* **31**:396, 1864.

tumor was soft and gelatinous and had all the characteristics of the echondrosis sphenoccipitalis described several years previously. Since then an increasing number of reports have appeared concerning this rather uncommon tumor. The first case reported in this country was that of Jelliffe and Larkin,<sup>9</sup> in 1912. There are now about one hundred cases of chordoma of all varieties on record. They have been reviewed from time to time, particularly by Jelliffe and Larkin, Daland,<sup>10</sup> Burrow and Stewart,<sup>11</sup> Eckel and Jacobs,<sup>12</sup> and Stewart and Morin.<sup>13</sup>

Because of the wide variation in the clinical manifestations accompanying these tumors, depending on the site and the direction of growth, they may be observed in almost any field in the practice of medicine. When the tumor is located at the upper end of the spine the presenting symptoms may lead the patient to the neu-

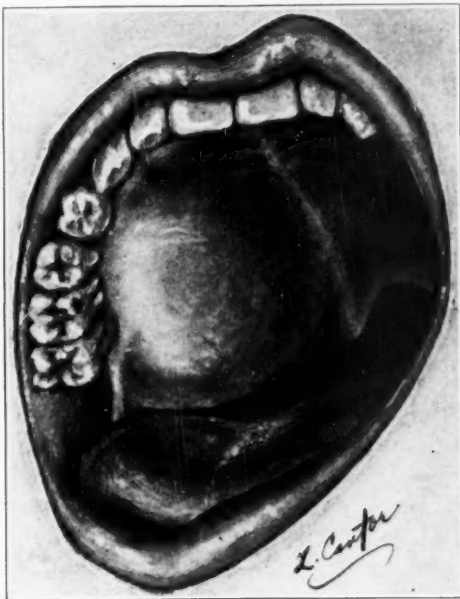


Fig. 1.—The tumor as seen inside the mouth. The right upper molars were pushed out of their sockets by the growth.

rologist, the ophthalmologist or the rhinolaryngologist. Disturbances along the vertebral column may come to the attention of the orthopedic surgeon, while tumors in the sacrococcygeal region are encountered by the proctologist or the abdominal surgeon. The published reports include cases classified clinically in

9. Jelliffe, S. E., and Larkin, J. H.: Malignant Chordoma Involving Brain and Spinal Cord, *J. Nerv. & Ment. Dis.* **39**:1 (Jan.) 1912.
10. Daland, E. M.: Chordoma, *Boston M. & S. J.* **180**:571 (May 22) 1919.
11. Burrow, J. le F., and Stewart, M. J.: Malignant Spheno-Occipital Chordoma, *J. Neurol. & Psychopath.* **4**:205 (Nov.) 1923.
12. Eckel, J. L., and Jacobs, W. F.: Malignant Spheno-Occipital Chordoma, *J. Nerv. & Ment. Dis.* **61**:471 (May) 1925.
13. Stewart, M. J., and Morin, J. E.: Chordoma, A Review, with Report of a New Sacro-Coccygeal Case, *J. Path. & Bact.* **29**:41 (Jan.) 1926.

each of these fields, making the recognition of chordoma a general, rather than a special, clinical problem.

Although these tumors may arise at any point along the vertebral column where notochordal remnants have been shown to exist, the great majority appear at the upper and lower extremities, and are accordingly designated as spheno-occipital and sacrococcygeal, respectively. The spheno-occipital group, by reason of the location of the tumor at or near the base of the brain, includes the cases which are most likely to present early and striking symptoms. The following record is, in general, typical of such cases.

#### REPORT OF CASE

*History.*—Mr. O. K., aged 58, an American, a blast-furnace worker, was first seen on June 18, 1930, when he complained of an aching pain over the right half of the face, of about six months' duration. It was gradual in onset and was



Fig. 2.—Echordosis physaliphora. A flat, mushroom-like mass of gelatinous notochordal tissue, attached by a slender pedicle to the middle of the dorsum sellae. (From Stewart and Morin.<sup>13</sup>)

first noted on arising in the morning. It would abate during the day, only to recur the following morning. A month after the onset of the pain he noted a decrease in visual acuity, which was more marked in the right eye. At this time there appeared small groups of pinhead-sized vesicles on the right upper lip, which disappeared in a week but were immediately followed by pain in the same place. The pain became progressively more severe and extensive until at the time he sought medical attention it involved the entire right half of the face. The skin was very tender, and he had been unable to secure any relief at home. The pain was aching in character, never sharp or shooting. He had lost 32 pounds (14.5 Kg.) in weight during the illness, but felt reasonably well, aside from the local difficulty, and had been working regularly. He had had sciatic neuritis in 1904, and acute iritis in the right eye in 1910 and in the left eye in 1915. Vision was gradually restored to normal, after which there was no difficulty until the present illness. Auditory acuity had been gradually diminishing for the past twenty years; this was probably related to his occupation. There had been no other important illness.

*Examination.*—The patient was white-haired, mentally alert and well oriented. Recent loss in weight was apparent from a lean appearance and somewhat flabby skin. The head showed no tender spots, scars or bone defects. The pupils were equal and of regular outline; the right reacted sluggishly to light, and the left normally; both reacted well in accommodation. There were diplopia on lateral deviation to the right and ptosis of the right lid. There was no exophthalmos or nystagmus. The scleras were clear, and the corneas were normal. Vision was

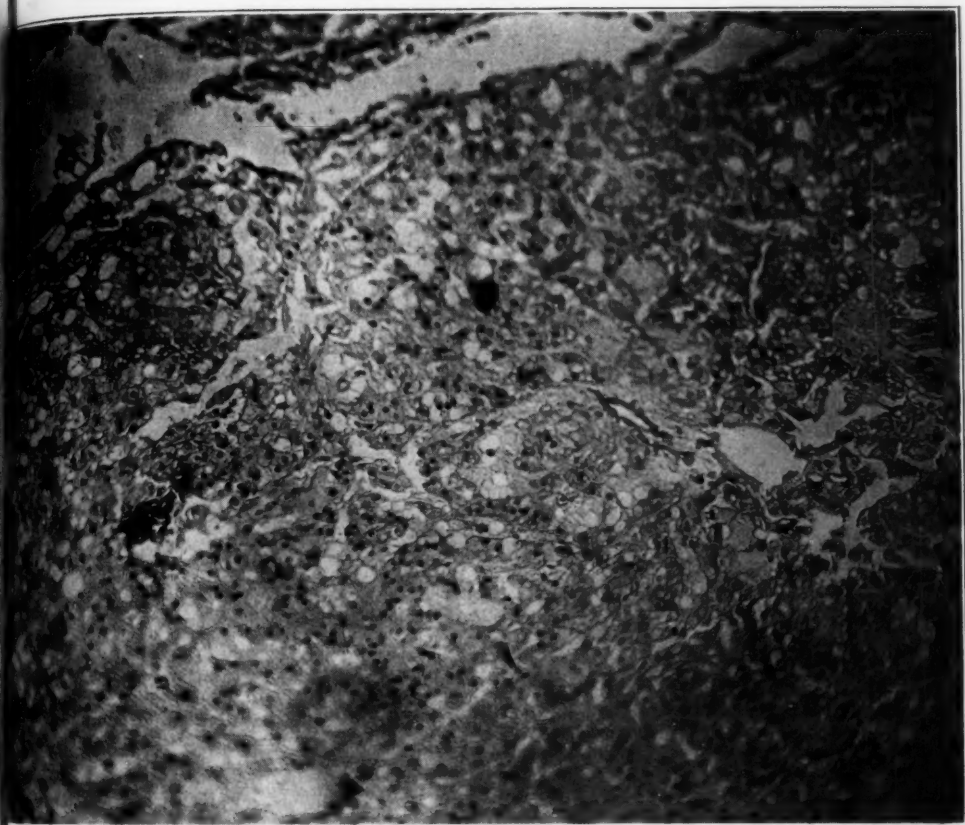


Fig. 3.—Photomicrograph showing the standlike arrangement of tumor cells. (Courtesy of Dr. Plinn Morse).

markedly impaired in the right eye, and slightly in the left. Ophthalmoscopically there was slight blurring of both nerve heads, but no choking; the vessels appeared normal. Hearing was somewhat diminished. The tympanums appeared normal. The nose was normal. The teeth appeared vital. The tongue protruded in the midline without tremor or atrophy. The palate appeared normal. There were diminished sensation over the right half of the face and weakness of the right facial muscles. There was no abnormality of the neck, or of the thoracic or abdominal viscera. The extremities were normal. The blood pressure was 98 systolic and 70 diastolic. There was no significant arteriosclerosis. Neurologic

examination gave negative results elsewhere over the body. The significant findings, therefore, included signs of impairment of the right second, third, fifth, sixth and seventh cranial nerves.

The urine was normal. The blood showed: hemoglobin, 100 per cent (Sahli); red cells, 4,860,000; white cells, 10,600; polymorphonuclears, 68 per cent, and no significant abnormality in the stained smear. Repeated Wassermann and Kahn

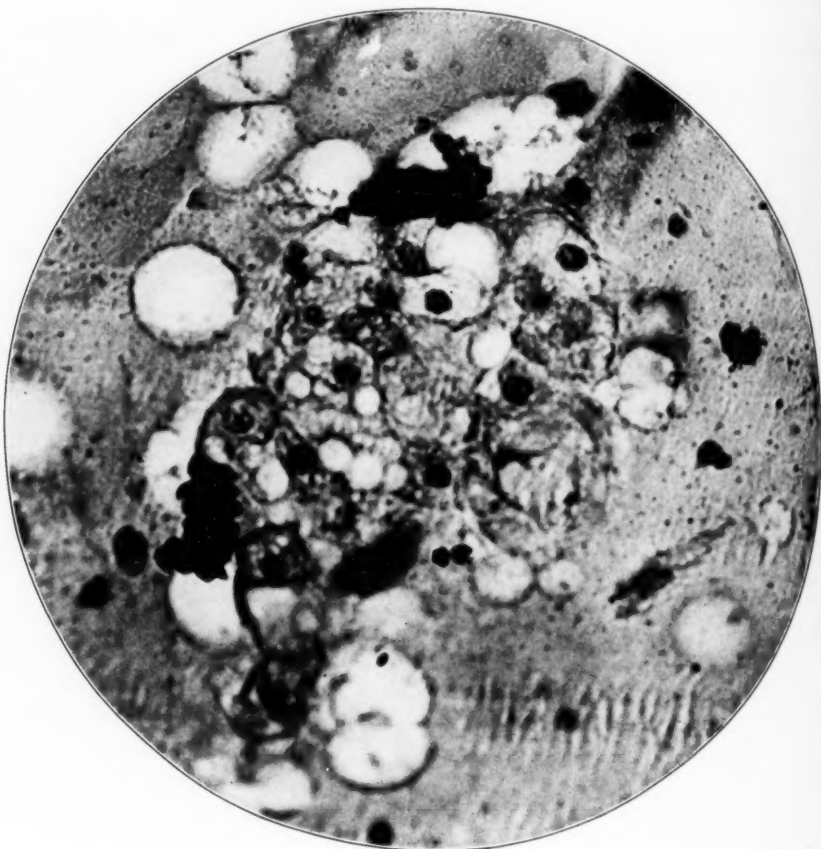


Fig. 4.—Photomicrograph showing physaliphorous cells. (Courtesy of Dr. Plinn Morse).

tests on both the blood and the spinal fluid were negative, and the spinal fluid was normal on other routine tests. Roentgen examination of the skull showed absence of the posterior clinoid processes, with some evidence of erosion of the base of the skull, suggesting a pituitary tumor. The temperature, pulse rate and respiratory rate were within normal limits. The pain could be only partially controlled by the usual remedies, and complete relief was obtained only from narcotics.

*Course.*—During a period of about two months there was little change in the man's condition. He refused all suggestions for surgical treatment. In September it was noted that the pulse was definitely slower than before, the rate varying

from 60 to 70. Vision in the right eye became progressively less and was totally lost. Ptosis of the right upper lid became more marked, and there was increasing pain in the region of the eyeball. The patient was not seen for about six months, until May, 1931, when a mass the size of a plum could be seen pushing into the oral cavity from the right palatal region. There was no ulceration of the overlying mucous membrane. The tumor protruded externally in the region of the zygomatic process of the maxillary bone, causing marked facial asymmetry. Externally the mass was firm but elastic. It was painless but slightly tender on pressure. The mandible was not involved in the growth. The skin, although stretched over the tumor, was intact. The pain, which previously had been present over the entire right side of the face, was limited to the orbit and parietal region; it was as severe and intractable as before. Examination showed total blindness of the right eye; the pupillary reflexes were absent. There was proptosis of the eyeball of about 1 cm., with neuroparalytic keratitis and conjunctivitis and complete external ophthalmoplegia. The left eye showed no change from the condition presented at the previous examination. Sensation was lost over the right half of the face. The right masseter muscle was very weak, and the right facial muscles were completely paralyzed. There was loss of taste over the right anterior portion of the tongue, and the tip deviated to the right. Hearing in the right ear was somewhat more impaired than in the left. The palate on the right was immobile, the soft tissue being bulged downward by the tumor, causing regurgitation of food and rendering speech almost unintelligible. Neurologic examination gave negative results elsewhere over the body. Weakness was marked and progressive. The pulse rate averaged 50. During the succeeding six weeks the tumor encroached farther and farther on the oral pharynx, aggravating the dysphagia. Death occurred on July 10, 1931.

*Autopsy.*—The important observations, and therefore the description, are limited to the head. There was a tumor on the right cheek, about 4 cm. in diameter. There were exophthalmos, marked keratitis and conjunctivitis in the right eye. The mouth was open, and a tumor from the right palatal region protruded into the oral cavity. The right upper molar teeth were missing. The brain was removed intact in the usual manner. A soft, mushy tumor tissue filled the right orbital and nasal cavities and the maxillary, ethmoid and sphenoid sinuses. It had destroyed most of the base of the skull. The zygomatic process of the temporal bone was completely replaced by the neoplasm. The tumor pressed against the frontal lobe of the right cerebral hemisphere, where it had caused a marked depression, but it had not metastasized to the brain. The blood vessels were congested, but no other definite changes were observed in the brain. The second, third, fourth, fifth, sixth and seventh nerves on the right side were involved in the tumor.

Microscopically, the tumor consisted of small lobules separated by rather loosely woven connective tissue septums containing numerous thin-walled blood vessels, which were dilated and contained red blood cells. Hemorrhages were seen in the perilobular tissue, but not in the parenchyma of the tumor. Small areas of calcification were also found in the septums, and within these were many lacunar spaces containing shrunken cells. The septums were thick and distinct over most of the lobules, measuring 60 microns or more. In some parts of the tumor, however, they were much thinned out. Numerous cells full of dark golden granules were found chiefly in the interstices of the connective tissue network. These were blood pigment granules.

The content of the lobules varied from richly cellular masses with scanty intercellular tissue to abundant intercellular homogeneous matrix in which were suspended tumor cells of vague outline. Strands of cells of more distinct outline

were also found in the matrix. The appearance of such areas gave the impression of a syncytium.

In the richly cellular areas the cells were arranged in columns passing in varying directions. The cells were polygonal for the most part and ranged in size from relatively small cells, 14 microns in diameter, to huge vacuolated cells three or four times that size. The nucleus, together with a small zone of cytoplasm, was suspended in the middle or at one side of the cell by a delicate reticular network of fibrils. Many of these vacuolated cells had vacuolated nuclei. These were the typical physaliphorous cells which are pathognomonic of chordoma. The degree of vacuolation varied from large numbers of cells with no vacuoles to cells that appeared to be a single large vacuole with no nucleus. Occasional small pools of homogeneous pale-staining mucoid material were found, as well as an occasional thin-walled vessel containing abundant red cells.

In the lobules the substance of which appeared to be syncytium the outlines of the cells were lost for the most part. The nuclei appeared suspended in this homogeneous pale-staining intercellular substance, which contained many vacuolar spaces. Many of the vacuoles contained shrunken cells the appearance of which resembled cartilage cells. In addition to the lacunar spaces, strands of cells of indistinct outline with pale-staining nuclei were found running through the mucoid tissue. No mitotic figures were seen.

No metastases were found in the lymph glands or other viscera.

#### COMMENT

This case illustrates well the salient clinical and pathologic features of chordoma—a slowly growing tumor, malignant by position and as a result of its locally invasive and destructive characteristics, especially with regard to bone, and seldom giving rise to metastases. The average duration of life of patients with sphenoccipital chordoma is two and six-tenths years after the onset of symptoms. However, in the case reported by Lemke<sup>14</sup> symptoms began twelve years before death, and in the case of pharyngeal chordoma reported by Fabricius-Møller<sup>15</sup> there were symptoms for seven years before operation and for five years afterward. Headache, dizziness and progressive failure of vision are often early symptoms and are accompanied or followed by palsies of the cranial nerves. Papilledema may occur; in the case of Thomas and Jumentié<sup>16</sup> it was the only sign present. Of the cranial nerves, the second is the most frequently involved. Various combinations of palsies are seen; that of palsies of the sixth and seventh nerves is the most common. Symptoms of bulbar palsy may be present from the first, or they may not appear until the growth of the tumor is far advanced. In spite of the common involvement of the sella turcica, signs of derangement of the pituitary gland are unusual. The exceptions to this observation are the cases of Lemke and Cushing,<sup>17</sup> in both of which the pituitary gland itself showed changes at autopsy. In Lemke's

14. Lemke, R.: Ein Fall von malignem Chordom der Schädelbasis, *Virchows Arch. f. path. Anat.* **238**:310, 1922.

15. Fabricius-Møller, J.: Chordoma of Retropharyngeal Region, *Hospitaltid.* **62**:849 (July 16) 1919.

16. Thomas, A., and Jumentié, J.: Un cas de chordome de la région sphenoccipitale, *Rev. neurol.* **39**:300, 1923.

17. Cushing, H.: *The Pituitary Body and Its Disorders*, Philadelphia, J. B. Lippincott Company, 1912, case 17; reviewed by Bailey, P., and Bagdasar, D.: *Am. J. Path.* **5**:439 (Sept.) 1929.

patient, polydipsia was a symptom, and in Cushing's there were notable gain in weight and loss of libido. A roentgenogram may show evidence of absorption of bone or the outline of the tumor. In the case reported by Alajouanine and his associates,<sup>18</sup> definite calcification was seen in the tumor on roentgen examination. In a few cases it was possible to make a histologic diagnosis by curetting or puncturing local extensions of the tumor at the base of the skull.

A most striking feature of chordomas is their locally destructive effect on bone. This was well illustrated in the present case, in which it was impossible to tell just where the tumor began and the skull ended. The whole mass being homogeneous, the only indication of the site of the skull was the somewhat gritty "feel" imparted to the palpating hand in that portion of the mass which had formerly been bone. The tumor not only had penetrated and destroyed the base of the skull and the maxillary bone but had invaded the orbit and the maxillary, ethmoid and sphenoid sinuses. Such widespread infiltration is not unusual, but invasion of the brain substance is rare, being reported in only one case (Lemke). Metastases are, less rare, particularly in the sacrococcygeal cases; they have been reported in at least six instances. Jelliffe and Larkin reported probable metastases in the spine in their case of sphenoid-occipital chordoma; sections of the metastatic areas could not be made, however, to verify the diagnosis. Mathias'<sup>19</sup> case resembled ours in that the tumor eroded through the frontal bone, making its appearance on the face. It not only involved the orbit and sinuses but, penetrating the bone, fungated on the surface.

Malignant chordomas are to be distinguished from the benign ecchondrosis physaliphora of Virchow, more aptly termed ecchordosis physaliphora by Stewart.<sup>20</sup> The latter are the small, jelly-like nodules occurring at the clivus blumenbachii; they are found in from 1 to 2 per cent of all autopsies (Ribbert), whereas malignant chordomas are rare. The two types of tumors are microscopically identical, but present contrasting appearances in the gross specimen and in the mode of growth. The non-neoplastic nodules of chordal tissue appear as small, translucent, gelatinous masses attached by a slender pedicle to the middle of the dorsum sellae. They project through an aperture in the dura and often become adherent to the pia covering the pons. They show no evidence of active growth and are vestiges of tissue left in situ as a result of a developmental arrest. The malignant chordoma, on the other hand, varies in its location from the occiput to the sacrum, and in its macroscopic appearance according to the degree of malignancy. The greater the amount of mucin the more benign the tumor, whereas the more cellular the growth the more malignant. Some of the malignant chordomas may resemble sarcomas very closely, as in the cases reported by Debernardi<sup>21</sup> and Hellmann.<sup>22</sup> The typical chordoma is well encapsulated and is separated into lobules by fibrous tissue trabeculae. Each lobule consists of gelatinous tissue. The consistency of

18. Alajouanine, de Martel, Oberling and Guillaume: Chordoma of Pituitary Body: Anatomic and Clinical Study, *Rev. neurol.* **1**:1221 (June) 1930.

19. Mathias: Ein Beitrag zur Lehre vom malignem Chordom, *Verhandl. d. deutsch. path. Gesellsch.* **19**:198 (April) 1923.

20. Stewart, M. J., and Burrow, J. le F.: Ecchordosis Physaliphora Sphenoid-Occipitalis, *J. Neurol. & Psychopath.* **4**:218 (Nov.) 1923.

21. Debernardi, L.: Cordoma sarcomatoso del sacro, *Arch. per le sc. med.* **37**:404, 1913.

22. Hellmann, K.: Ueber ein malignes Chordom des Nasenrachenraumes, *Verhandl. d. Gesellsch. deutsch. Hals-, Nasen- u. Ohrenärzte* **1**:3, 1921.

the tumor varies with the thickness of the interlobular septums, those with thick septums appearing firm. In the later stages the septums may break down, causing the formation of an amorphous, gelatinous mass.

#### SUMMARY

1. Chordomas arise from remnants of the notochord. They may occur at any point along the vertebral column, but are most frequent at the upper and lower extremities.

2. A case of spheno-occipital chordoma, in which autopsy was performed, is reported. The clinical and pathologic findings were characteristic and included many of the usual features of brain tumors in general, with a rather slow progression and multiple palsies of the cranial nerves.

3. An outstanding characteristic of chordomas is the readiness with which they invade bone.

4. They are malignant by position and by their locally invasive quality. They seldom metastasize and rarely invade the brain itself. Although they often involve the region about the pituitary gland, there are seldom any signs of pituitary dysfunction.

5. Diagnostic differentiation of chordomas from other varieties of intracranial tumors cannot be made clinically. Pathologically the appearances are distinctive.

6. Malignant chordomas are to be distinguished from the benign variety of notochordal remnants—*ecchordosis physaliphora*—which occur at the clivus and cause no symptoms.

## DWARFISM AND OCULAR DEFECTS IN HEREDOFAMILIAL DISEASE OF THE CENTRAL NERVOUS SYSTEM

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The interest in the cases described in this paper is twofold: (1) They present an unclassified type of heredofamilial disease of the central nervous system; (2) they show singular somatic manifestations associated with the neurologic manifestations. The study was based on examination of the accessible members of a Greek Jewish family. In two generations four members of the family were found who presented neurologic symptoms; one of them was manifestly ill; another showed latent neurologic symptoms, as well as obvious somatic anomalies; the third and fourth manifested chiefly latent neurologic symptoms.

### REPORT OF CASES

**CASE 1.—History.**—Sophie S., aged 16, had parents who were blood relatives, her father being her mother's uncle. She was born at full term, by normal delivery, and weighed  $6\frac{1}{2}$  pounds (2,954.35 Gm.). As an infant she was considered "small and weak." Development was somewhat slow. Dentition began at the age of 1 year; she learned to walk at the age of  $1\frac{1}{2}$  and to talk at the age of 2.

The present complaints were "nervousness and shaking of the hands." The mother stated that these symptoms appeared at the age of 10 years and grew progressively worse, without remissions or exacerbations. The patient had menstruated for three or four days every four weeks since the age of 13; she missed only two periods in three years. In the last few months, however, menstruation had become scanty.

**Examination.**—The gait was somewhat staggering, with a broad base. The Romberg sign was weakly positive. There were tremor of the head, marked intention tremor of both upper extremities and bilateral adiadokokinesis. All deep reflexes were increased and equal bilaterally. The abdominal reflexes could not be elicited on the right side; they were diminished on the left, the upper reflex being more lively than the lower. There was a positive Babinski sign. There was weakness of the lower two thirds of the left facial nerve. There was undulatory nystagmus of both eyes, observable in all positions. The speech was scanning.

There was stunting of growth, the height being  $53\frac{1}{2}$  inches (135.8 cm.); the span of the outstretched arms was  $52\frac{1}{2}$  inches (133.3 cm.); the distance from the symphysis pubis to the soles was  $26\frac{1}{2}$  inches (67.2 cm.). The normal minimal

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Read at a meeting of the New York Neurological Society, Dec. 6, 1932.

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height for this age is  $61\frac{1}{10}$  inches (155.25 cm.). (The standards of height referred to in this paper are those established by Engelbach.<sup>1</sup> They are necessarily somewhat arbitrary.) The breasts were well developed. The shape of the nose was suggestive of the saddle-back type. The eyebrows were heavy and met in the midline. The hair line was low and approached the eyebrows in the temporal region. There was an increased amount of lanugo over the extremities and in the sacral region. Both eyes showed hypermetropia of 6 diopters.

The patient was moronic. Both the ideational and the motor intelligence quotient were 63. She also showed emotional instability, being resistive and tearful and then cheerful and jocular.

The basal metabolic rate and the sugar tolerance curve were normal. The Wassermann test of the blood and of the spinal fluid was negative. Roentgen examination showed normal ossification. The sella turcica was considered about 20 per cent undersized.

*Diagnosis.*—As this was the first patient examined, diagnosis offered considerable difficulty. The neurologic symptoms, consisting chiefly of cerebellar and pyramidal tract signs, were suggestive of disseminated sclerosis. However, the fact that the patient was only 16 years of age and that her symptoms, which were first noticed at the age of 10, had shown no remissions or acute exacerbations made a diagnosis of disseminated sclerosis improbable. Another problem was the connection between the neurologic symptoms, the stunting in growth, the refractive error and the anomalies of distribution of hair. Congenital syphilis of the central nervous system was ruled out by the negative result of the Wassermann test and by the absence of all suggestive history or signs. The third possibility was that the condition was an unclassified type of heredofamilial disease.

*CASE 2.*—Sarah S., aged 6, a younger sister of Sophie S., had an identical developmental history. She learned to walk at the age of  $1\frac{1}{2}$  years and to talk at 2. At the time of examination the mother thought that the patient was in good health, except that she considered her undersized.

*Examination.*—The patient walked with a somewhat staggering gait, on a broad base. The Romberg sign was weakly positive. She could not maintain a good erect posture; lordosis of the lumbar spine would appear while she stood. Both arms showed an intention tremor, which was more marked in the right arm. Pseudo-athetoid movements were observable in the fingers of the right hand. All deep reflexes were increased and equal bilaterally. All abdominal reflexes were diminished. Babinski's sign was positive on the right side, and questionable on the left. Chaddock's sign was positive. The eyes showed undulatory nystagmus in all positions.

The patient was stunted in growth, the height being 37 inches (93.9 cm.), the span of the outstretched arms,  $35\frac{1}{2}$  inches (90.1 cm.), and the distance from the symphysis pubis to the soles,  $17\frac{1}{3}$  inches (43.3 cm.). (The normal minimal height for this age is  $43\frac{1}{10}$  inches [109.5 cm.].) The nose was of the saddle-back type, the eyes were somewhat slanting, and there was slight epicanthus. There was an increased amount of lanugo over the extremities and in the sacral region. Both eyes showed hypermetropia of 7.5 diopters, and blue patches were observed on the right sclera.

An intelligence test showed a dull normal ideational intelligence quotient (75) and a borderline motor intelligence quotient (70).

Laboratory tests and roentgen examination of the skull and of the long bones gave negative results.

1. Engelbach, William: Growth Hormone, *Endocrinology* **16**:6 (Jan.-Feb.) 1932.

*Comment.*—This patient showed definite cerebellar and pyramidal tract signs, stunting in growth, anomalies of distribution of hair and marked hypermetropia—a symptom complex similar to that of her sister.

At the time of writing, both patients have been under observation for a year and a half without any noticeable change in the symptoms. The patient in case 2 has grown  $1\frac{1}{2}$  inches (3.7 cm.).

CASE 3.—Sam S., aged 42, a paternal uncle of the patients in cases 1 and 2, made no complaints.



A, the patient in case 1; B, the patient in case 2.

*Examination.*—All deep reflexes were increased and equal bilaterally. The abdominal reflexes were easily elicited on the left side. The right upper abdominal reflex was diminished, and the right lower reflex could not be elicited. Examination of the cranial nerves showed definite weakness of the lower two thirds of the left facial nerve. There was a bilateral weakness of the sixth nerve with deficiency of convergence; the right eye fixed and the left diverged. There were no other abnormal neurologic findings.

The patient was not stunted in growth but was short, his height being 60 inches (152.4 cm.), the span of the outstretched arms,  $62\frac{3}{4}$  inches (158.4 cm.), and the distance from the symphysis pubis to the soles, 30 inches (76.2 cm.). Both eyes showed hypermetropia of 1 diopter.

Performance tests showed a dull normal intelligence quotient (75).

All laboratory tests gave negative results.

*Comment.*—This patient showed slight bilateral signs of involvement of the pyramidal tract and some disturbances in ocular movements. He was short in stature. Both eyes showed hypermetropia.

CASE 4.—Esther L., aged 23, a maternal aunt of the patients in cases 1 and 2, complained of poor vision.

*Examination.*—Both eyes showed undulatory nystagmus in all positions. This was the only abnormal neurologic finding.

The patient was slightly stunted in growth, her height being 59 inches (150 cm.), the span of the outstretched arms, 61 inches (155 cm.), and the distance from the symphysis pubis to the soles, 30 inches (76.2 cm.). The eyebrows were heavy and met in the midline. Both eyes showed congenital cataract, myopia of 10 diopters and myopic changes in the eyegrounds.

*Comment.*—The abnormal neurologic finding (nystagmus) in this case is of doubtful importance. The condition may have been purely optic.

#### OTHER MEMBERS OF THE FAMILY

The patients whose cases have been described were the only members of the family who presented abnormal neurologic symptoms. However, study of other members with regard to growth, distribution of hair and refractive errors is of interest. It does not seem necessary to give a detailed description of all the persons examined; I shall mention only the general features that have a bearing on the problem. Most members of the family have been examined. About the others fairly accurate information was gained from photographs and reports given by those examined. It should be repeated that the parents of the patients in cases 1 and 2 were blood relatives, the father being the mother's uncle.

According to statements of the family and a photograph, the paternal grandmother (i. e., the maternal great grandmother) of the patients in cases 1 and 2 was of very small stature, possibly being a dwarf; she was hardly taller than the patient in case 1. The paternal grandfather was allegedly tall and well built. Neither of them was manifestly ill.

The siblings of the patients in cases 3 and 4 (twelve, including the parents of the patients in cases 1 and 2) were all short, with the exception of one man, who was not examined. However, they did not show marked stunting in growth. The women showed a tendency toward the same anomalies of growth of hair as were noted in the patients in cases 1 and 2. All of these members who were examined had hypermetropia, the most marked being 4.5 diopters, and the mildest, 1 diopter.

The intelligence quotients varied from 57 to 100. The intelligence of these people could be tested only with the greatest difficulty (by Mrs. R. Wells, psychologist of the New York Post-Graduate Medical School and Hospital). All were immigrants and had a limited knowledge of English. The results of the tests had to be interpreted with much reservation, the chief reliance being placed on the motor intelligence (performance time), which on the whole was in harmony with the impression gained from contact with the subjects.

In contrast with the many uniform characteristics of the parents, uncles and aunts of the patients in cases 1 and 2, the cousins (twelve) showed wide divergences both in the somatic and in the mental sphere, resembling, almost without exception, the parents that married into the family. Thus, to mention two extremes, the height of one cousin was 46 inches (116.84 cm.) at the age of 9 (normal, from

49 $\frac{1}{10}$  to 52 $\frac{1}{10}$  inches [124.7 to 133.6 cm.] and that of another was 67 inches (170.2 cm.) at the age of 16 (normal, from 61 $\frac{1}{10}$  to 65 $\frac{1}{10}$  inches [155.25 to 165.8 cm.]). The intelligence quotients ranged between 149 and 63. In one family all the children were tall and had high intelligence quotients; they resembled the mother who married into the family. In another, all were of the adiposogenital type (one of the boys had undescended testes) and had uniformly low intelligence quotients; they resembled the father who married into the family.

The patients in cases 1 and 2 had one sister and one brother. It is interesting that the sister, aged 12 years, although her features resembled those of her mother, was well grown, being 57 inches (144.8 cm.) tall (normal height for her age, from 55 $\frac{1}{10}$  to 59 $\frac{1}{10}$  inches [141.2 to 151.5 cm.]); she had a superior intelligence quotient (114) and no errors in optical refraction. In other words, she differed markedly from her sisters (resembling her grandfather?). The brother, aged 10 years, resembled the family type in appearance; he was 51 inches (129.5 cm.) tall (normal height for his age, from 51 $\frac{1}{10}$  to 55 inches [130.5 to 140.2 cm.]). He had an intelligence quotient of 81 and a hypermetropia of 4 diopters in both eyes.

#### COMMENT

It seems obvious that the somatic and mental traits of the patients whose cases are described and of their relatives are partly racial and partly familial. The wide divergence of traits among the cousins of the patients in cases 1 and 2 is explainable by two assumptions: (1) the recessive nature of the familial characteristics and (2) the influence of the new environment, the parents having all been immigrants. The close resemblance between the parents who married into the family and their offspring confirms the first assumption. The second assumption is also probably correct. It is in harmony with the frequent observation that the children of immigrants are apt to differ from their parents. The traits in cases 1 and 2 due to consanguinity of the parents are exaggerations of the normal and latent pathologic (abiotrophic) racial and familial traits in the previous generation.

A condition like that in cases 1 and 2, so far as could be determined, has never been described in the literature. As to the neurologic findings, the general tendency, ever since the work of Jendrassik,<sup>2</sup> has been to regard heredofamilial diseases of the central nervous system as one large group, termed heredodegeneration, the various syndromes of which often appear in combination in one patient or in various members of one family. A combination of syndromes in the same patient is illustrated by the cases showing Friedreich's disease in association with muscular dystrophy which were reported by Jendrassik;<sup>3</sup> a variety of syndromes in the same family, by cases such as were described by Ferguson and Critchley.<sup>4</sup> Jendrassik also stated that many possible combinations of symptoms in heredofamilial diseases have been described, and that there are many which have not been described. In the cases reported here the condition resembled disseminated sclerosis closely, except that there were no remissions. It cannot be considered typical Friedreich's ataxia, because of the lack of bony deformities and the presence and the increase of all deep reflexes; nor can it be considered Marie's ataxia (in the

2. Jendrassik, in Lewandowsky: *Handbuch der Neurologie*, Berlin, Julius Springer, 1911, vol. 2, p. 340.

3. Jendrassik,<sup>2</sup> p. 396.

4. Ferguson, F. R., and Critchley, MacDonald: *Heredo-Familial Diseases Resembling Multiple Sclerosis*, *Brain* 52:203 (July) 1929.

limited sense), because of the age of the patients (below 20), and the presence of signs of involvement of the pyramidal tract. In the patients of Ferguson and Critchley<sup>4</sup> symptoms developed between the ages of 35 and 45; most of the patients had parkinsonian symptoms. Robinson and Robinson<sup>5</sup> described eight cases of multiple sclerosis in three generations (no remissions!). The symptoms developed between the ages of 30 and 40. Schob<sup>6</sup> described multiple sclerosis in a brother and a sister; the symptoms developed in adult years and showed definite remissions; autopsy was performed.

Our cases, as well as those of Scheftel,<sup>7</sup> bear a close resemblance to the cases described by Pelizäus and by Merzbacher,<sup>8</sup> and might be considered as belonging to that group. The tracts involved, judging by the symptoms, are similar, and so is the early onset of the disease. The symptoms in the cases of Pelizäus and Merzbacher were much more severe. There were marked retardation in development and severe degrees of spastic paraplegia. In Merzbacher's series there was one abortive case in which slight facial weakness was exhibited.<sup>9</sup> However, the patient was the only allegedly healthy member of the family examined by him, and it is possible that other abortive cases would have been found had he examined other members.

As to the combination of stunted growth and other somatic anomalies with diseases of the central nervous system, the case reported by Holmes<sup>10</sup> should be mentioned. His patient, however, showed cerebellar signs only, and presented marked endocrine disturbance, manifested by small genitals, sparseness of hair, etc. The patient in the case described by Falta<sup>11</sup> showed signs of muscular dystrophy, infantilism, deficiency of ossification, cryptorchidism and a large tongue. Janney<sup>12</sup> described similar cases. The case described by Joffrey<sup>13</sup> was one of juvenile paralysis agitans (?; the diagnosis was made in presenile times), combined with obvious endocrine disturbance.

The patients in cases 1 and 2 were built proportionately. Roentgen examination showed no disturbance of ossification, and the basal metabolic rate was normal. In case 1 there were slight menstrual irregularities, which, however, were of doubtful significance in consideration of the patient's age. One can, therefore, regard the condition in these two cases as dwarfism due to faulty anlage. It should be pointed out that the nature of dwarfism and the relation of the various forms to one another are still debated. Transitional forms exist (Falta<sup>14</sup>).

5. Robinson, G. W., and Robinson, G. W., Jr.: Eight Cases of Multiple Sclerosis in Three Generations, *J. A. M. A.* **92**:892 (March 16) 1929.

6. Schob: Multiple Sclerose bei Geschwistern, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **80**:56, 1922-1923.

7. Scheftel, Yetta: Pelizäus-Merzbacher Disease, *J. Nerv. & Ment. Dis.* **74**:175, 1931.

8. Merzbacher, L.: *Ztschr. f. d. ges. Neurol. u. Psychiat.* **3**:1, 1910.

9. Merzbacher,<sup>8</sup> p. 57.

10. Holmes, Gordon: Familial Degeneration of Cerebellum, *Brain* **30**:467, 1907.

11. Falta, in Mohr and Staehelin: *Handbuch der inneren Medizin*, Berlin, Julius Springer, 1927, vol. 4, pt. 2, p. 1315.

12. Janney, N. W.: Muscular Dystrophy, *Arch. Int. Med.* **21**:88 (Feb.) 1918.

13. Joffrey: Paralyse générale juvénile, *Encéphale* **7**:1, 1908.

14. Falta, W.: *Endocrine Diseases*, translated and edited by A. E. Garrod, ed. 3, Philadelphia, P. Blakiston's Son & Co., p. 490.

In many of the previously mentioned cases of Pelizäus and Merzbacher the patients were myopic. Somatically, all were well developed, with the exception of one (case 10). This patient, who was bedridden all her life and whose osseous system showed atrophy, osteoporosis, osteomalacia, rachitis and severe deformities, was evidently suffering from secondary dwarfism. If our cases are considered as belonging to Merzbacher's group, interest lies in: (1) the presence of abortive types in the first generation and (2) the appearance of dwarfism in two children of the second generation who were born of consanguineous parents.

These cases are unique in that they showed a combination of dwarfism with a heredofamilial disease of the central nervous system resembling multiple sclerosis; but, on the other hand, they are of more general implication. More and more data are being accumulated to show that in heredofamilial diseases of the central nervous system other organ systems are also involved. I am unable to decide, however, whether the basic disturbance in my patients was a metabolic one, such as Sachs,<sup>15</sup> for example, suggested for amaurotic idiocy, and Janney,<sup>12</sup> for muscular dystrophy.

#### SUMMARY

Four cases of heredofamilial disease resembling multiple sclerosis are described, all occurring in members of a family of Greek Jewish extraction. The patients in two of the cases (daughters of consanguineous parents) showed, in combination with cerebellar and pyramidal tract signs, stunted growth, marked refractive errors and slight anomalies of growth and distribution of hair. The symptoms may be regarded as a result of an exaggeration of the recessive abiotrophic tendencies present in the generation to which the patients in the other two cases belonged. The cases are unique in the special combination of symptoms but are of general interest in that they show involvement of other structures in addition to a disturbance of the central nervous system.

15. Sachs, B.: Amaurotic Family Idiocy and General Lipoid Degeneration, *Arch. Neurol. & Psychiat.* **21**:247 (Feb.) 1929.

## SPECIAL ARTICLE

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### TRAINING OF THE NEUROLOGIST, THE NEURO- PSYCHIATRIST AND THE PEDIATRICIAN

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Neuropsychiatry, it would seem, is doing for itself what pediatrics began to do about five years ago: to take stock and to orient its place in the fields of medical education and practice. As chairman of a group of pediatricians who undertook this work and who are still engaged in it, I regard the invitation to discuss the question "What does the pediatrician expect from the neurologist and psychiatrist?" as an opportunity not to be refused.

While the partitioning of medicine into special fields has been one of the chief factors in the tremendous growth of the medical sciences, at the same time it has brought about problems which have forced the subject of specialism and specialties into the foreground. There is no question but that specialization has been greatly overdone, particularly in relation to the practice of medicine. Moreover, the various specialties are built on quite different foundations. From the standpoint of medical education, the four basic clinical fields are medicine, surgery, obstetrics and pediatrics. The specialties either center around some particular anatomic system, as the genito-urinary, or around some particular disease, as tuberculosis. From the standpoint of medical practice, however, surgery is in reality a specialized therapeutic technic. The surgical specialty groups, as urology or ophthalmology, have their chief if not only justification in a still more highly classified type of diagnostic and therapeutic technic which it takes years to acquire. The same holds true for the groups which center about some particular disease.

The so-called medical specialties, as neurology, are in a somewhat different position. Neuropsychiatry—may I frankly state the general attitude of physicians toward it without raising the question of the validity of the point of view—has been regarded more as a diagnostic specialty. Perhaps in this lies the explanation of the rapid growth of neurologic surgery as an entity which is apparently upsetting some of my friends who have specialized in neurology. Pediatrics, from the standpoint of a specialty, is in an even more peculiar situation than is neurology. As this is a discussion of the relationship between neuropsychiatry and pediatrics, it is necessary to picture briefly the present conception and scope of pediatrics in the scheme of medical education

and practice, as it is on this conception—at least from the pediatrician's point of view—that the relationship is dependent. Pediatrics, unlike any other limited medical field, centers about an age period. It is the fact that one is dealing with the child, a growing, constantly changing and maturing organism, that gives pediatrics the only justification for existing as a limited, restricted field of medicine. It is not a question of disease or of pathology or of specialized therapeutic technic. So far as the practice of medicine in its strict sense is concerned, pediatrics is the practice of general medicine limited to an age period. Any one who looks on the pediatrician simply as a "baby feeder" or as a physician who deals with the diseases of childhood holds an erroneous and limited conception of present day pediatrics. Perhaps the definition of pediatrics given in one of the reports of the committee on pediatric medical education will express the scope and field of pediatrics as satisfactorily as can be done: "Pediatrics is that branch of the medical sciences which has to do with the factors influencing the growth and development of individuals from birth to maturity."

This definition centralizes pediatrics on the study of the developing organism. Nutrition (the feeding of infants) is considered as a means of obtaining normal growth. Disease is of importance as it interferes to a greater or lesser degree with normal growth and development. To the pediatrician the prevention of disease is more important than its cure. Normal growth and development necessarily imply mental as well as physical health and development. The pediatrician must take into consideration, not only specific pathologic processes and diseases, but also the entire group of environmental factors, of which the home and school are examples, which influence the growth and development of the maturing organism.

Pediatrics differs from internal medicine in that it is concerned with the growing, developing organism, while internal medicine is concerned with maturity and degeneration. Each age period has its own problems. From the standpoint of pathology and therapeutics, the pediatricians are in fact "general practitioners" and frankly admit it. This brings them into a certain relationship with all the more definitely restricted fields of special practice, as neuropsychiatry, and, in a broad sense, their relationship to any one of these fields is in many respects similar to their relationship to all. What it looks for is help in special conditions the diagnosis or treatment of which calls for knowledge or skill such as cannot be expected of one who must have considerable knowledge of the entire field of medicine. This is quite simply the relationship between the specialist and the general practitioner. The relationship breaks down in that the pediatrician considers the total child, a point of view which he has learned is essential, while the specialist, with his intensive knowledge of some limited field, usually

regards the existing situation from the narrower point of view of his own field of interest. So much may be said in a general way. For a more specific discussion it is best to consider neurology and psychiatry as separate entities, although it is recognized that such a separation does not always exist.

#### NEUROLOGY AND PEDIATRICS

The neurologic conditions of childhood fall into four main groups: trauma and hemorrhage occurring at birth, new growths, the acute infectious processes and the epilepsies. In addition, there is a miscellaneous lot of uncommon and rare conditions which may be considered without discussion as problems of neurology rather than of pediatrics.

The prevention of trauma and hemorrhage occurring at birth concerns the obstetrician chiefly, but once these have occurred, recognition of them and immediate relief are pediatric problems. Moreover, the nutritional problem of the new-born infant is as important as the problem of local damage. The therapy of late stages or results is orthopedic rather than neurologic or pediatric.

New growths bring up another problem. The recognition that symptoms suggestive of cerebral tumor are occurring in a child necessitates the making of a decision by the pediatrician. He recognizes that the only possibility of help lies in neurologic surgery. Should he refer the child to the neurologist for further study or to the trained neurologic surgeon? If he is sufficiently suspicious of what is taking place he feels, as a rule, that the earlier the case is in the hands of the surgeon the better, and sees no cause for delay and extra study by a middleman. He knows that, regardless of the opinion of the neurologist, the neurologic surgeon must follow his own conclusions as to localization and decide on the plan of operation. That is outside the province of either the pediatrician or the neurologist. The only drawback in referring the problem directly to the neurologic surgeon is one that relates to referring any problem to the surgeon: The surgeon as a rule handles the patient as a temporary therapeutic problem. As surgical cases are usually emergency cases, one cannot expect much more. On the other hand, the very nature of a surgical neurologic problem often creates environmental, physical and mental or psychologic problems, or may lead to problems which continue throughout childhood and into adult life. In this way the condition may be carried beyond the field of pediatrics and surgery into that of neuropsychiatry.

The majority of conditions involving the nervous system in childhood are acute infectious processes. The important point is that they are acute infections, not that they involve the nervous system. Involvement of the nervous system is only a part of the pathology. The treatment of an infection is by one of two means: the use of some

specific method of therapy, or, when this is unknown, the maintenance of life until the natural immunologic forces come into play. The development of specific methods of therapy is a problem that only the bacteriologist and immunologist can solve. Whether such a person is working in a laboratory of hygiene, a pediatric clinic or a neurologic institute is a matter of secondary importance, as he is fundamentally neither a pediatrician nor a neurologist.

The pediatrician regards the clinical aspects of the acute infections as belonging to his field. It would be as logical to consider scarlet fever or measles as belonging to the field of dermatology, or acute follicular tonsillitis to the field of otolaryngology, as to consider poliomyelitis as a neurologic problem. Seemingly only relatively few cases of the latter involve the central nervous system, at least to any recognizable degree. Where, if a separation of the acute infections was made, would varicella be placed, a condition in which the virus produces changes in the spinal fluid but in which the obvious lesion is in the skin? Syphilis in the infant involves the central nervous system in at least 25 per cent of the cases; so far as life and death is concerned it is the simultaneous involvement of the visceral organs that is important. Chorea is only one and often not the most important expression of a rheumatic infection.

Leaving aside such academic discussion, there is a very practical side to the question of the acute infectious processes. The pediatrician or general practitioner is called to see a sick child with an acute infection. The condition may be any one of a multitude of infections. There are many symptoms common to all, and often he must make a differential diagnosis from only slight suggestive findings and institute specific therapy, if it is available. There is one basic principle involving all forms of specific therapy: The earlier in the course of the disease the therapy is used the better the results and the less chance of permanent residual processes. The vast majority of pediatricians and general practitioners have no time and the opportunity is not often available to call for the help of a "specialist" in such a situation. Consequently the pediatric clinic, into whose hands, as a rule, falls the teaching of a large part of the clinical aspects of the acute infectious processes, has the responsibility of the teaching of the few which involve the nervous system, as well as those involving the skin or lungs, for example. The pediatrician recognizes that there is nothing peculiar in the pathology of any of these diseases which makes it a "disease of childhood," except that in the young growing organism immunity has not been established.

Unfortunately, many of the acute infections involving the nervous system are not headed off before permanent damage is done, leaving paralysis, muscular weakness, mental retardation and other conditions.

The problem then becomes one of restoring function. Mechanical appliances, the suturing of nerves, the transplanting of tendons, exercises and other methods of treatment are in order. These often call for a highly specialized type of surgical technic, and the problems become orthopedic rather than neurologic or pediatric.

The question of the epilepsies is not so clearcut. After many years during which drugs were used as the chief method of treatment a number of investigators turned to metabolic studies. While this movement has been initiated in part by the neurologic group, it is a field that has attracted the attention of the pediatricians. As a result of their interest in metabolism, many physicians in the pediatric clinics are expert chemists and physiologists. As many of the problems of normal and abnormal metabolism in infancy and childhood have been rapidly solved in recent years, it is but natural that these trained workers should have turned to a study of other conditions, among them epilepsy. Whether the treatment of certain selected types of epilepsy by ketogenesis and altered water metabolism is the solution of the problem is as yet uncertain. It is natural, however, that such studies should be undertaken by those qualified in the basic sciences to carry on such work properly. It seems to me immaterial whether these studies are carried out by neurologists or by pediatricians.

Unusual or rare diseases of the nervous system in childhood belong properly in the field of neurology. Degenerative lesions are rare in childhood, and the pediatrician knows little about them. He cannot expect to understand or help these obscure and complicated neurologic conditions without the aid of the neurologist. But this group of diseases forms only a small fragment of the neurologic conditions of childhood. As in the case of physicians in other fields, the pediatrician must realize his limitations and depend on those who have special training and knowledge in a more restricted field.

Only one conclusion can be drawn by the pediatrician, and that is that pediatrics does not expect much from nor depend much on neurology. This statement is based, of course, on a consideration of the total field of pediatrics.

#### PEDIATRICS AND PSYCHIATRY

When psychiatry is considered the story is quite different. Here one is dealing with matters that are less clearly defined and do not permit of such definite classification. In saying this I am using the term psychiatry in a very broad sense, including psychology, psychiatry in a strict sense and that rather important-sounding subject called "child guidance." That all of these have been jumbled together in many minds is unquestionably true. It is also true, however, that they are interrelated.

One of the most interesting phenomena of recent years has been the discovery by workers in many fields of clinical medicine that the

child plays a very important part in the medical picture of their respective limited fields. Pediatricians have been aware of this for many years. The first concerted move involving infancy and childhood was the one started years ago by pediatricians and others to reduce the mortality in infancy and childhood. It was based on mixed motives: humanitarian, economic and political. The modern phase of this—a general organized child hygiene movement—started about thirty years ago. Unfortunately, the zeal of the enthusiast got ahead of the facts and the medical direction, and the movement passed to a large extent into the hands of the lay worker and the propagandist. It was assumed by nurses, nutritionists and executives of health agencies, who led the public to believe that by diet, health education service, serums, vitamins and the like the physical problems of the infant and child would be rendered nonexistent. The dissemination of such knowledge regarding health has been followed by a wave of oversolicitude almost as dangerous to the child as ignorance. In turn, the child became the center of attack of the tuberculosis enthusiast, the cardiac specialist, the social hygienist and other groups with a limited specialized interest. What might be termed the latest phase of this movement, the mental hygiene movement among children, has now been reached. Despite the attacks of enthusiasts who look on the child with myopic eyes, the pediatrician fails to wax violently enthusiastic over each new wave, for he realizes that he must consider the total child and weigh his problems from all points of view.

It has been assumed that there is something new in mental hygiene and that a wonderful discovery has been made in a field neglected by the pediatrician and even by the psychiatrist. This is scarcely the fact. One can find many statements in pediatric books of the last century which show that the mental side of the child's growth and development has been considered. Perhaps a more accurate criticism would be that the pediatrician's attitude toward these matters has been secondary and instinctive rather than primary and formulated in the sense that the physical hygiene of the infant and child has been formulated.

There has been in pediatrics a widespread interest in the mental side of childhood. Pediatricians have been looking for facts which they could use in dealing with parents in their daily work and could pass on to medical students. They have turned to the psychiatrists and, I regret to say, they have not had the help for which they have hoped. My own feeling is that the psychiatrists have not agreed on facts to give them. The pediatricians have found schools and theories in direct opposition. When one hears from a certain extreme group that "every worker with children should be psychoanalyzed," one rather crosses one's fingers.

The pediatrician has been told further that mental growth and development belong not to the field either of psychiatry or of pediatrics,

but to the "clinical psychologist;" in other words, that a whole new group of workers in the field of childhood should be formed whose point of view would necessarily be very limited. Common sense and experience tell one that this is wrong. Moreover, in turning to psychology to find this miraculous thing that the new group would have to offer, one finds enough difference of opinion, argument, disagreement and contention to make a miniature World War. When one hears the ductless glands talked about so glibly by persons who cannot accurately locate them and who have no idea as to the nature of their secretions, one begins to question not only their wisdom but their intellectual integrity. There are, of course, many splendid workers in this field who are doing much to clarify the psychology of childhood.

The pediatrician knows that the totality of the child must be considered and not the child divided up into segregated fields of interest. While one realizes that the mental side of a child's growth and development is important, unfortunately one finds, instead of the definite scientific data available on the physical side, a mass of material on the mental side contradictory and theoretical on which one is unable to pass sound judgment. If there is one definite duty which the psychiatrist owes the pediatrician and the practicing physician it is that of clarifying this situation. One looks on the psychiatrist as the physician whose function it is to know the mind in its normal as well as in its abnormal development.

The "child guidance" movement is one that interests the pediatrician intensely, and I believe that it is more nearly related to pediatrics as a whole than to psychiatry. Pediatricians have watched it closely and have taken part in it with the hope that it will eventually be a pathway to better things. Those who for many years have been closely associated with the child hygiene movement have seen a marked parallelism between the two. The chief fault of the child guidance movement has seemingly been its intense desire to prove something rather than to find out something and to look on its methods as fixed rather than experimental. Not many years ago I heard one of the chief exponents of the movement state that the "child guidance clinic would eliminate child delinquency in a few years." He would be the first to laugh at such a statement today. In child guidance, as was the case in earlier infant welfare work, there is a confusion between principles and methods. The child guidance clinic is only a method. When one pictures the evolution and change of the infant welfare clinic or health center in the past twenty years, the description of the present child guidance clinic as a "classic" unit brings a smile. I have every reason to believe that the child guidance clinic is being and will continue to be an important factor in bringing about a better understanding and in turn a better handling of the problems of childhood. Its chief fault has

been its isolation. As the pediatricians have come to see the problem, its chief value lies not in its existence as a separate unit or field but rather in the possibilities for its close incorporation into the complete medical program for the child. While isolated units may be needed for specific purposes, as in the schools for educational problems or in association with juvenile courts, the most important place of the clinic is in the medical school, in intimate association with medical education. Only in this way can it influence the thought and attitude of physicians, and in the ultimate analysis this is the only method by which help in problems of conduct and behavior can be given to the millions of children in America. Child guidance clinics, like infant welfare clinics, can reach directly only a very small number of persons.

The question is frequently discussed whether the child guidance clinic belongs to the field of pediatrics or to that of psychiatry. As yet the answer is not clear, and only time and experience will tell. My own feeling is that for practical purposes its organization into pediatrics is the solution.

This leads back to the fundamental question of the relation between the two fields and what the pediatrician expects from the psychiatrist. One can only express a point of view. Mine is based on certain relationships extending over a number of years. Myself a pediatrician and actively associated with a progressive pediatric department of a medical school, I have been chairman of the board of a child guidance clinic under the direction of a competent and broad-minded psychiatrist. This clinic, which started as a separate unit, has been merged with a children's hospital which is the pediatric clinic of the medical school. In addition, an office relationship of many years' standing with the head of the psychiatric department of the medical school has led to such matters being the topic of endless discussion and thought. This biographic information has been given to show that what has been reached in the way of opinion is not a hastily conceived idea nor an impractical one.

There are many problems of conduct and behavior in infancy and childhood which, although involving the psychology of childhood, cannot be classed by any stretch of imagination as psychiatric. While they lead in some instances, as in the case of habits connected with food, to a hindering of normal physical development, and in others, as in the case of temper tantrums or enuresis, to the development of undesirable personality, they certainly are not indicative of abnormal mental development. They are the result of wrong training and the effects of the environment surrounding the child. That such conditions may cause more distress and trouble than actual illness is recognized, and once having developed they may be exceedingly difficult to correct. Such problems belong directly to the field of pediatrics, and the pediatrician

must be constantly on the alert to prevent their occurrence by advice in the same way that he must concern himself with the care of the skin, clothing and the like. That such conditions are forerunners of psychoses, an impression which the mental hygiene movement has to a certain extent created, even though this may not have been intended, is not in line with the facts. The maladjustments of the home and school may or may not be of serious significance. Different causes may lead to apparently similar reactions. The personality and adjustment problems of the older child are even more important. They may be simple in nature and relatively unimportant, or they may be the early expression of serious difficulties. When there is any suggestion that a potential psychosis is present, the problem is one to be turned over to the psychiatrist as soon as possible. In case of doubt on the part of the pediatrician, the problem should be considered a psychiatric one and the help of the psychiatrist should be sought.

The child guidance clinic has overlapped the two fields. Part of the problems which it has attempted to handle are distinctly pediatric, while part lie in the realm of psychiatry. The important phase of the pediatric type of problem is the preventive. The child guidance clinic, on the other hand, is distinctly a therapeutic method, except in its general educational aspects. There has been, let it be frankly admitted, a certain need for expediency in child guidance work. As the conception of the field of pediatrics has been changing and adjusting, the importance of child guidance work, particularly of a preventive type, has been recognized more rapidly than knowledge has been available for utilization. The pediatrician has turned to the psychologist and psychiatrist and has found a mass of contradictory theories, ideas and therapeutic measures which have left him in bewilderment. Until the psychiatrist can distinguish the important from the unimportant, the true from the false, the fact from the theory and formulate his findings, and until he can separate the child who presents psychiatric problems, the pediatrician must be cautious in plunging into a movement which promises at present a great deal more than it can accomplish.

The pediatrician needs the help of the psychiatrist. In the same way that he must distinguish the inflamed ear that he can treat safely from the one which necessitates treatment by the otolaryngologist, or the case of pyelitis which will respond to simple medical therapy from that which requires the skilled therapeutic technic of the urologic surgeon, so he must be able to distinguish the problems in conduct, personality or education which can easily be adjusted or corrected from those which represent potential psychoses. So far these data have not been satisfactorily formulated by the psychiatrist or made available as a whole to the pediatrician. It should be possible to segregate two clearly defined fields, one pediatric and one psychiatric. Between the

two lies, as in all fields of medicine, a borderland that can be satisfactorily handled only by close cooperation and understanding.

The line that has been drawn between the neurologist and the psychiatrist is perhaps a too rigid one. The differentiation has been made for the sake of simplicity in discussion. The neuropsychiatrist should attack a specific problem in a child from the broad point of view of training, inheritance and environment, as well as of disease. The neuropsychiatrist, moreover, has, or should have, a better insight into the future of the individual child than the pediatrician, as he deals with adults as well as with children. The behavior or conduct problems of children, as well as organic lesions, which are potential problems of adult life should be much better defined and formulated than they are at present. This is knowledge that can come to the pediatrician only from the neuropsychiatrist, and in this relation there is an opportunity for a much closer correlation between the two fields than ordinarily exists at present.

The mere fact that a discussion such as this is invited, that the pediatricians at the White House Conference on Child Health and Protection had a special committee of the two groups which reported on their interrelated problems, that the psychiatrists and psychologists are writing for the pediatric journals and that such contributions are welcomed and sought by the pediatricians, augurs well for the establishment of sound and sane relationships between the two fields and are indications that the pediatrician looks for and expects help which the psychiatrist is ready to give.

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## Abstracts from Current Literature

JUBILEUM EDITION IN HONOR OF DR. MAX NONNES'  
SEVENTIETH BIRTHDAY. DEUTSCHE ZTSCHR. F.  
NERVENH., 1931, VOLS. 117-119

HYPOPHYSEAL CACHEXIA IN ARTERIOSCLEROSIS OF THE BRAIN. A. BOSTROEM,  
Munich, Germany.

Three types of hypophyseal cachexia may be distinguished. One may be called the symptomatic type. Here the destruction of the anterior lobe of the hypophysis may be caused by a tumor, gumma or abscess or by tuberculosis. The second type, Simmond's disease, occurs in women. This type is caused by embolic and thrombotic processes taking place in connection with pregnancy. After parturition, the menses fail to return, general weakness gradually sets in, sensitiveness to cold develops, the mental activity may suffer, and there is slowing of motility. The complex of symptoms in the first group may be similar to that in the second group if the anterior lobe of the hypophysis becomes damaged. Other characteristic symptoms are loss of teeth and disappearance of hair, especially in the axillary area. The third type includes a group of cases in which the hypophyseal symptoms form only part of a general pluriglandular involvement. It is not always possible to draw a sharp line between the so-called pluriglandular condition and Simmonds' disease, since even in the latter disease atrophy of other glands of internal secretion is often found. Some are inclined to class hypophyseal cachexia with pluriglandular insufficiency. Bostroem, however, is inclined to consider hypophyseal cachexia a separate disease, and agrees with Reye that the gradual increase of cachexia in Simmonds' disease must cause atrophy in other glands of internal secretion.

In hypophyseal cachexia proper, the first damage apparently is caused by a disease process resulting from confinement, regardless of whether it is an embolus, a thrombus or an exhausted function of a labile hypophysis. In younger persons, the cachexia gives an impression of premature senility. The diagnosis is not difficult in cases in which the symptoms are characteristic, namely, pronounced weakness, pallor of the face, a spongelike skin, falling out of the teeth and loss of hair. It is important to recognize these cases in the earlier stages when treatment may be of considerable benefit. The cachexia often develops slowly. Some women complain of weakness after confinement and remain undernourished. In these cases, one should think of a possible disturbance of the anterior lobe of the hypophysis.

Diagnostic difficulties are also encountered in cases complicated by symptoms due to other diseases. More difficult are the cases in which the development of the symptoms is atypical. This is especially true in women who are past the climacteric period and in whom the symptoms develop in a comparatively short time. Bostroem reports a case of his own.

A woman, past 60 years, at the age of 23 had given birth to a child that lived for three months. There were no other pregnancies. At the age of 40 she had articular rheumatism, with complete recovery; the menopause occurred at 48, with no particular disturbances. The symptoms under discussion set in suddenly, with loss of the use of the right leg. There was no loss of consciousness. Physical examination revealed general debility; the face was wrinkled, the teeth were missing, and the patient looked much older than her age; the skin was dry; the hair of the head and of the axillary area was nearly gone; there was a systolic murmur at the apex; the blood pressure was not increased; the hemoglobin measured 72 per cent; a slight anemia was present; the urine was normal. The

neurologic findings were, briefly: right facial palsy; the tongue placed slightly to the right; no Babinski sign; the calf musculature tender to pressure, and indistinct speech. In a few days, the symptoms almost disappeared, but there remained a certain somnolence, fatigability and general apathy. The diagnosis made was hypophyseal cachexia and cerebral arteriosclerosis.

Post mortem there were found a moderate arteriosclerosis in the cerebral blood vessels, a fresh subdural hemorrhage on the left, a bean-sized softening in the head of the right caudate nucleus and small lesions in the left putamen. Macroscopically, the hypophysis was small and shrunken and resembled a connective tissue bag. Microscopically, the anterior lobe had nearly disappeared; nothing remained of the middle lobe, and very little of the posterior lobe. There were a considerable number of large cysts in the hypophysis, apparently caused by the breaking up of the hypophyseal tissue. In some places necrotic areas were present; there was proliferation of connective tissue which included also the capsule. The cause of the atrophic process was not determined. Arteriosclerosis could not be held responsible. The process was not recent; it had lasted at least for three or more years.

Bostroem was impressed by the fact that although the atrophy of the hypophysis had lasted for three years or longer, the patient showed no serious hypophyseal symptoms. The loss of the teeth and hair was apparently not of recent origin; on the other hand, general weakness had not been present until late. Perhaps the explanation lies in the fact that some portion of the anterior lobe still remained, a condition to which Simmonds had called attention. He was of the opinion that cachexia does not set in until the entire organ is lost; as long as sufficient tissue remains to function, it is capable of preventing the appearance of symptoms. The loss of the teeth and hair in this case was apparently of long standing. Possibly these disturbances may be brought on by a relatively mild insufficiency of the anterior lobe of the hypophysis. If this is so, it would be of considerable importance in recognizing the disease in an early stage, at a time when organotherapy may be of value.

Another point for consideration in this case is the pregnancy which occurred at 23 and the menopause at 48. The disease could therefore not have had any relation to pregnancy, and up to the time of the menopause, at least, the function of the hypophysis must have been satisfactory. What, then, was the cause of the atrophy of the hypophysis? Arteriosclerosis can be excluded by the histologic observations. That abuse of alcohol and tobacco in this case can be held responsible is questionable. A relationship to the articular rheumatism from which she suffered at the age of 40 is doubtful. No definite cause can be found in this case; the other organs of the body were not examined post mortem. Having in mind the histologic findings in Simmonds' disease, one might think that the pregnancy brought about a mild injury to the hypophysis which was not sufficient to interfere entirely with its function. When circulatory disturbances set in, cachexia developed.

In nearly all cases of Simmonds' disease, in addition to physical manifestations, there are mental disturbances, although not all the mental disturbances should be regarded as the result of the hypophyseal insufficiency. Some symptoms appear so regularly, however, that they must have some relation to the diseased hypophysis. Here should be mentioned the apparent apathy, which seems to be a result of general weakness, the difficulty of decision, and in typical cases the loss of libido and potency.

ARACHNOIDITIS ADHAESIVA CIRCUMSCRIPTA. B. BROUWER, Amsterdam, The Netherlands.

Circumscribed adhesive arachnoiditis has been found by many investigators not only to follow diseases and traumatic injuries of the spine, but also to be a primary disease with an independent nosology. The clinical symptoms of this disease are similar to those of extramedullary tumor, and operative procedures may be of benefit. Formerly, the condition was spoken of as circumscribed spinal serous meningitis, or as cystic spinal serous meningitis. In the newer literature, the

pathologic process in the arachnoid is recognized. This is due to studies of the spinal fluid and to the findings in roentgenograms after injection of iodized poppy seed oil 40 per cent. The disease can now be diagnosed early, and the location can be established if the medullary functional disturbance has not advanced too far. The arachnoid space is also the route for the transportation of micro-organisms, and there are many reasons for assuming a centripetal inflammation—from without toward the medulla. Brouwer reports 7 cases of this type, with various etiologic factors.

CASE 1.—A man, aged 34, soon after recovering from an attack of amebic dysentery, began to complain of peculiar sensations in the legs, which gradually increased in severity. At the same time, there developed a feeling of constriction around the knee joints, with frequent sensations as if an electric current shot through the leg. Gradually, walking became difficult, and the patient tired easily and dragged his feet when walking. Occasionally, there was pain in the lumbar area, and at night there were twitchings in the legs.

Examination revealed an incomplete Brown-Séquard paralysis; both legs were paretic, the right more than the left. There was increased tonus on the right, with positive Babinski and Oppenheim signs. Occasionally, contractions occurred in the musculature of the leg, and slight disturbances were noticed in the sensations of touch, pain and temperature. The abdominal reflexes were weak on the right. There were no sphincter disturbances. The spinal fluid showed a normal pressure (from 160 to 170 mm. of water); with light pressure on the veins in the neck, the pressure rose to 285; however, the return to the normal was rather slow; a strong pressure on the veins caused a normal rise and fall. The fluid was clear; the Nonne-Apelt and Pandy tests were positive; the Wassermann reaction was negative; there was no pleocytosis. A second puncture, a week later, gave the same pressure, but no globulin was found. An injection of iodized oil revealed no obstruction.

A year later, the weakness of the legs had become more marked, although the pain had stopped; pain in the back had become more marked, and the fifth thoracic spine was painful to pressure. The Queckenstedt test again showed a slow return to normal, and the Nonne-Apelt and Pandy tests were negative. Iodized oil was again injected suboccipitally; some remained at the sixth thoracic vertebra, and a small strip was noticed at the level of the seventh thoracic vertebra. The slow, progressive development of the symptoms led to the assumption of an extra-medullary tumor.

A laminectomy was done from the sixth to ninth thoracic vertebrae. No tumor was found, but the arachnoid was swollen and under pressure; on cutting into it, a large quantity of fluid escaped.

The postoperative course was uneventful. The patient recovered rapidly.

Brouwer mentions that Foster Kennedy had reported that spinal arachnoiditis may produce the picture of Brown-Séquard paralysis, thus making the diagnosis even more difficult. Among the acute infectious diseases in which arachnoiditis may develop, cerebrospinal meningitis takes the lead; it is not known that amebic dysentery may bring it on. Therapeutic results may be excellent.

CASE 2.—A man, aged 45, had complained of a sharp pain and cramps in the right leg for more than a year; they had come on suddenly. He was treated for acute sciatica, at first with some benefit, but the pain soon returned. On examination the Lasègue sign was positive on the right. There was pain when he lay on his back, but it disappeared when he lay on his abdomen. There was no atrophy or paresis in the leg, pressure points along the course of the sciatic nerve or sensory disturbance. At times there were an Oppenheim sign on the left and the suggestion of a Babinski sign on the right. Lumbar puncture revealed: a pressure of 95 mm. of water; with light pressure over the jugular veins, no rise in the manometer; with strong pressure, a rise to 120, the movement being slow; with compression of the abdomen, a rise to 410 mm. of water, the fall being rapid. The fluid was clear; the Nonne-Apelt, Pandy and Wassermann tests were negative. There was no increase in cells. There apparently was more than a sciatic involve-

ment. One and five-tenths cubic centimeters of iodized oil was injected suboccipitally; most of it passed down to the sacrum, but a small portion remained at the level of the eleventh thoracic vertebra.

Laminectomy between the ninth thoracic and second lumbar vertebrae was done. The arachnoid was swollen and opaque, and when it was opened considerable fluid escaped. Aside from a mild pain in the right leg, the patient recovered completely.

No definite etiologic factor was discovered in this case. Brouwer thinks that an arthritic disposition can be assumed to be the cause. The patient's mother suffered from rheumatism, and the patient himself, six years before, had had an inflammatory swelling of the sternoclavicular joint. Leriche and Barré pointed out that arachnoiditis circumscripta may be accompanied by arthritic changes in the vertebrae; but they failed to state whether the arachnoiditis is the result of the arthritis or whether both diseases have a common cause. Experience gained from extramedullary tumors indicates that at times they actually are capable of producing secondary local arthritic changes in the vertebrae.

This case also teaches the importance of examination with iodized oil. Sensory disturbances were lacking. The sciatic pain suggested a disturbance in the lower part of the cord, perhaps in the cauda. The injections of iodized oil therefore offer an advance in the differential diagnosis of lesions of the cord.

The surgical results in arachnoiditis generally are not so good as in extramedullary tumors, partly because intramedullary changes may be present at the same time. Vincent therefore recommended roentgen and radium treatment after laminectomy, together with internal vaccine medication.

Case 3 was that of a boy, aged 8 years, in whom, one year after he had passed through a severe attack of epidemic cerebrospinal meningitis, difficulty in walking developed. Later he had scarlet fever. Since then the motility in both lower extremities had become worse. Examination revealed a high grade of paralysis in both legs. No disturbances were present in the upper extremities or the head. The Babinski and Oppenheim signs were positive on both sides; the lower abdominal reflexes were not obtained; cutaneous sensibility showed some changes reaching up to the trunk. No fluid was obtained on lumbar puncture. Suboccipital injection of iodized oil showed that it remained at the level of the eighth thoracic vertebra. A second injection by the lumbar route showed shadows of iodized oil at the second and first lumbar and twelfth thoracic vertebrae. This indicated an extensive adhesion. Laminectomy has not yet been done.

This observation indicates the importance of the injection of iodized oil, by both the descending and the ascending route, in determining the localization of extramedullary growths. It becomes even more important in spinal arachnoiditis, since here the process is often diffuse. The ascending route should be tried only in cases of suspected complete obstruction, since the iodized oil has been found months afterward at the base of the skull or in the ventricles. Swedish investigators have found that iodine dissolved in oil of sessamum is least irritating to the meninges; therefore they use larger quantities and inject as much as 10 cc., claiming by this method to be able to detect finer details.

CASE 4.—A man, aged 49, after a severe attack of the grip complicated by thrombosis in both legs and an embolus of the lung, began to suffer pain in the lower part of the back, which gradually moved up to between the shoulder blades. The intensity of the pain was variable. Shortly afterward, there developed ataxia of the lower extremities, twitchings of the legs, urinary and intestinal disturbances and abnormal sensations in the legs. Motility in the lower extremities was greatly disturbed. The patient could not stand on his feet; the muscular sense in the joints of the toes was nearly lost; the same was true of the sense of vibration; cutaneous sensibility was disturbed for all qualities, reaching the level of the seventh thoracic segment on the left and the eighth thoracic segment on the right. The left knee reflex was lost; the right was diminished; the abdominal and cremasteric reflexes were not obtained; on the left, there was a suggestion of a Babinski sign. A lumbar puncture disclosed xanthochromia, marked increase of globulin and no cells. Only a few drops of fluid were obtained; hence, the Queckenstedt test could not be

applied. A suboccipital injection of iodized oil showed that most of the substance remained at the level of the sixth thoracic vertebra.

A laminectomy was performed, taking in the fourth to eighth thoracic vertebrae. The dura and epidural tissue were much thickened; the arachnoid was white, dull and not transparent. When the upper part of the arachnoid was cut into, there was an escape of fluid. The arachnoid was adherent to the pia. Although the postoperative course was complicated by infection, the patient's condition gradually improved, and motility partly returned. On the other hand, he showed the syndrome of a combined tract disease.

In this case, the toxic-infectious disease was responsible not only for the circumscribed pachymeningitis and leptomeningitis, but most likely also for intramedullary changes. Even in such cases, favorable therapeutic results may be obtained.

CASE 5.—A boy, aged 17, with a furuncle in the neck, was seized with chills, fever, vomiting and pain in the left lumbar region, radiating to the left shoulder. He looked septic. Soon afterward symptoms of myelitis developed, with pain along the spine which he could distinguish from the other pain. The lower extremities became paretic, the left being the worse. The sensations of touch and pain became involved in the lower half of the body, with an indefinite boundary line over the trunk. The tendon reflexes of the lower extremities were increased; ankle clonus was present on both sides; Babinski, Oppenheim, Rossolimo and Chaddock signs were positive on both sides, and the middle and lower abdominal reflexes were lost. Lumbar puncture gave a pressure of 150 mm. of water. With light pressure over the jugular veins, the pressure rose to 290 mm., but the rise and the fall took place slowly. With strong pressure over the neck, the pressure rose to 480 mm. of water; the fall was much too slow and reached only to 200. A suboccipital injection of iodized oil disclosed a block in the area of the ninth thoracic vertebra. Laminectomy was done from the seventh to eleventh thoracic vertebrae. There was a thickening of the dura and of the epidural tissue. In the area of the seventh thoracic vertebra, there was a normal pulsation of the dura. The thickened tissue, which apparently embraced the arachnoid and perhaps also the pia and was adherent to the cord, was removed. The patient died two days later. Postmortem examination was limited to the section of the cord on which laminectomy had been done.

Histologic examination showed a lesion in the middle of the posterior columns. Apparently this was the place where the inflammatory hyperplastic membrane was adherent to the cord. In this area there was also meningeal thickening, with peripheral myelitis that extended above and below the area. The slides gave the impression that the intramedullary changes were caused by the leptomeningeal process.

The importance of this case is that a furuncle was the primary cause of the disturbance.

CASE 6.—A man, aged 46, complained of dull pain in the lower part of the back, which after a while subsided. Later there developed stiffness in the legs, which made walking difficult. Urination was at times difficult. The patient had always been well; he said that he had not had a syphilitic infection. Examination revealed some weakness of the legs; abnormal vibratory sense in the legs; stiffness of the knees; short steps; increased tonus in the lower extremities; absence of ataxia; absence of abdominal reflexes; cremasteric reflexes, and positive Babinski and Rossolimo signs. The spinal fluid pressure was between 70 and 75 mm. of water; with light and strong pressure over the jugular veins, there was no change in the pressure. With abdominal pressure, the pressure rose to 500 mm. and quickly sank back. Xanthochromia was present, and globulin was greatly increased. There were no cells. The Wassermann reaction of the blood was twice negative and that of the spinal fluid was twice positive.

The diagnosis lay between a syphilitic combined spinal column disease and tumor of the cord. Iodized oil, injected by the ascending route, remained at the fifth thoracic level. Antisyphilitic remedies for many weeks brought no relief. Laminectomy

tomy was therefore performed. The transverse processes of the third, fourth and fifth thoracic vertebrae were removed. The dura was unchanged, but an arachnoid cyst was present at the level of the fifth thoracic vertebra, and adhesions were present between the dura and the arachnoid. The postoperative course was uneventful. Antisyphilitic treatment was given during convalescence; the patient soon recovered completely.

That syphilis may cause arachnoiditis is well known. In this case, a syphilitic genesis cannot be accepted with certainty. Here, too, however, an operative procedure was successful. Arachnoid cysts caused by tuberculous inflammation have been described by Gerstmann and others.

CASE 7.—A man, aged 37, had sustained a fracture at the base of the skull, with abducens paralysis, fracture of a vertebra and several fractures of the extremities in a fall eighteen years before. A year later he returned to work, although with limited capacity. Nine years after the accident he began to feel occasional pain in the umbilical area, with occasional sharp pains in the legs and numbness in the feet. Four years later the right leg began to feel weak, and a year later also the left leg. Six months before admission the symptoms grew worse. The legs were stiff and he could not walk so well as before. On examination there were found: a kyphoscoliosis in the ninth thoracic area; spastic paraparesis, with increased reflexes and tonus in the lower extremities; a Babinski sign on the left; absence of abdominal reflexes; diminished cutaneous sensibility for all qualities over the twelfth dorsal to the fourth lateral vertebra. A Queckenstedt test showed a very small and slow rise in the pressure of the spinal fluid. With pressure over the abdomen, the pressure rose to 500 mm. of water; the Nonne-Apelt and Pandy reactions were positive. There was no increase in cells. A suboccipital injection of iodized oil showed a block at the level of the tenth thoracic vertebra.

A laminectomy was performed. At the eleventh thoracic level there was a circumscribed pachymeningitis. The dura was smooth, but the arachnoid was discolored, edematous and gelatinous; it could easily be separated from the cord. The sensory disturbances disappeared; the patient recovered from most of the symptoms and was able to walk with the assistance of a cane. Later, pain in the legs again appeared; walking became difficult, and urinary disturbances set in. A lumbar puncture again revealed a disturbance in the passage of the spinal fluid. Diathermy was applied.

The important point in this case is that the arachnoid disturbance developed many years after the accident. Stookey pointed out that the normal movement of the cord is interfered with by adhesions of the arachnoid. The cord pulsates with each breath. At the point of adhesion the cord is held fixed, while above and below this point it makes normal excursions. It thus causes a mild trauma.

Observations in the 7 cases agree with Stookey's conception that the arachnoid and the pachymeninges sustain an injury as a result of trauma and that the adhesion takes place soon after. Mauss and Krüger described many cases of injuries to the cord occurring during the war under the name of meningitis serosa circumscripta, and likewise attributed them to mechanical influences. They also pointed out that new blood vessels often develop in these cases. The proliferated connective tissue in the arachnoid presses on the blood vessels, and in this way may produce circulatory disturbances in the cord.

Brouwer calls attention to the difficulties in differentiating clinically between circumscribed spinal arachnoiditis and extramedullary tumor. If there is a history of an acute infection, one should think of the former possibility. In tumors, alternating symptoms are observed, while case 1 shows that in spinal arachnoiditis the symptoms may be progressive and of slow development.

Of practical importance is the fact that tumors of the cord often are accompanied by arachnoid adhesions. Brouwer has recently observed 2 cases of interest. In the first case, after a trauma, there developed an arthritis of the cervical vertebrae and the right shoulder; gradually there appeared symptoms pointing to disturbances of the cervical cord. Laminectomy disclosed a circumscribed arachnoiditis. After the adhesions were separated, the cord failed to pulsate. Further exploration

revealed a tumor in the anterior wall of the vertebral canal. In the second case, an arachnoiditis was found in the thoracic area, and a tumor two segments above. Harbitz and Lossius recently showed that arachnoid disturbances may also be caused by a tumor lying at quite a distance. Odin, Runström and Lindblom pointed out that there are mild cases of arachnoiditis in which the patients suffer pain in the back and in the extremities. Often they show mild medullary disturbances, and examination of the arachnoid space reveals slight disturbances in the flow of the spinal fluid.

In conclusion, Brouwer points out that determination of the hydrodynamic relations in the cerebrospinal fluid and investigation with opaque substances have established that spinal arachnoiditis *circumscripta* occurs more frequently than was formerly believed. The etiologic factors in the 7 cases reported are also of considerable interest.

ACUTE MULTIPLE SCLEROSIS. HANS DEMME, Hamburg, Germany.

To those who attempt to draw conclusions concerning the pathogenesis of multiple sclerosis from the anatomic changes, the cases of so-called acute multiple sclerosis are of special interest, since in them one may expect to observe the earliest anatomic manifestations and thus to get a better insight into the genetic problem. Müller differentiated multiple sclerosis sharply from acute disseminated encephalomyelitis. On this point, Marburg observed that at best there can be only a quantitative difference. It is not possible to draw a sharp line. Many cases have since been reported; at times they have been described as acute disseminated encephalomyelitis, and at times as acute multiple sclerosis. Anton, Wohlwill, Finkelnburg, Fränkel and Jakob, Oppenheim, Greutzfeldt, Henneberg and Pette came to the conclusion that neither clinically nor anatomically is it possible to distinguish acute disseminated encephalomyelitis from acute multiple sclerosis. Redlich came out strongly for differentiating these diseases, however, although he admitted that a sharp line often cannot be drawn.

Pette, from a clinical and anatomic study of 3 cases, was able to show the imperceptible transition between acute disseminated encephalomyelitis and chronic multiple sclerosis. Verf recently described 2 very acute cases. One patient died after seven days, and one after nine days. Demme reports an acute case in which the patient died three weeks after paralysis had set in. The history of this case, briefly, is:

A man, aged 33, suddenly became ill, with high fever and a heavy feeling in both legs. After three days the fever disappeared, leaving him with a drawing pain in the arms and legs. Three weeks later, dizziness set in; eight days later a flaccid paralysis of both legs suddenly appeared, with disturbance of the bladder. At that time, the left pupil was larger than the right, and there were slight meningitis, spastic paresis of the upper extremities, flaccid paraplegia of the lower extremities, loss of the abdominal reflexes and considerable sensory disturbance in the lower extremities. The Wassermann reaction of the blood and that of the spinal fluid were negative. There was an increase of albumin in the spinal fluid, with an increase in cells and a mastic reaction. In the course of the next few days nystagmus and ptosis in the right eye developed. Pneumonia next developed, and the patient died twelve days later.

The clinical course alone permitted a diagnosis to be made. The spastic paresis of the upper extremities, the flaccid paralysis of the lower extremities and the bladder disturbance pointed to a disseminated process in the central nervous system. The findings in the spinal fluid indicated an inflammatory process.

Anatomic examination revealed macroscopically, from the pons downward, circumscribed reddish discolorations in the gray nuclei and in the cord, and a wedge-shaped lesion in the white substance of the cervical cord. Histologically, there were numerous extensive lesions, mostly in the cord and in the medulla. The white substance was mostly but not exclusively involved. In the pons and cerebellum were large lesions. In the cerebellum the lesions were sharply limited. In the area of the substantia nigra there were large, infiltrated lesions. Toward the basal ganglia and the hemispheres the pathologic condition diminished in

intensity. The myelin sheath showed patches of destruction in the cord, medulla and pons. Some lesions involved nearly the entire cross-section of the cord; at times they were symmetrical. The white substance was more often affected. The large lesions in the cord were comparatively sharply defined from their surroundings, forming at the border a kind of wall. This wall was composed mainly of glial elements, mixed with some lymphocytes and macrophages. The center of the lesion was composed mainly of fatty granular cells. Microglia were present in large number. Hortega elements were also present, with a lesser number of oligodendroglia. The blood vessels were infiltrated with lymphocytes and plasma cells. There was no hemorrhage. With the Bielschowsky stain, the axis cylinders were preserved in the lesions, but in the larger lesions they were spread out and swollen. Many of the ganglion cells in the center of the lesion showed acute cell destruction, such as swelling, vacuolation and colliquefaction. In addition to the large lesions, there were small areas of glial accumulation and vascular proliferation throughout the cord.

Similar lesions were present in the medulla. They were found mainly ventral to the olive and mainly in the white substance, as is frequent in multiple sclerosis. There were large lesions in the pons and many lesions in the cerebellum. In the substantia nigra and in the basal ganglia there was some vascular infiltration. In the hemispheres there were a few vascular infiltrations and glial accumulations. A lesion was present at the chiasm.

It is to be noted that at no place were the lesions present near the lateral ventricles.

The anatomic findings explain clearly the clinical symptoms. Whether this case should be classed as one of acute disseminated encephalomyelitis or as one of acute multiple sclerosis cannot be determined either from the clinical or from the anatomic findings. Clinically, it has more the picture of an acute disseminated encephalomyelitis; the rapid development of the symptoms after an acute infectious disease, the absence of visual disturbances and the rapid fatal termination without remission speak for this diagnosis. But a similar relapse may take place in chronic multiple sclerosis.

Nor is it possible to decide the question on the basis of the anatomic findings when these diseases are considered as separate entities, as at present they must be. On the whole, the condition appears to resemble multiple sclerosis more. Side by side are found acute and old lesions, sharply bordered off from the adjacent tissue. Again, the axis cylinders remained for the most part unaffected, while the myelin sheath was destroyed.

A fact of interest is the relation of the lesion to the cerebrospinal fluid system and to the blood vessels. Aside from a few lesions bordering on the fissures of the cord and a few at the periphery, and thus involving the meninges of the medulla and pons, there was no topographic relation between the lesions and the cerebrospinal fluid system. The lateral ventricles were free from any involvement. On the other hand, the vascular system was especially involved. The capillaries and especially the precapillaries were notably affected. The infiltration of the blood vessels consisted mainly of lymphocytes and plasma cells, followed by a reaction of the glia around the blood vessels. The blood vessels were affected only for a certain distance. It seems that the lesions had origin in the vascular system and not in the cerebrospinal fluid system. Demme is of the opinion that not all cases of acute encephalomyelitis are to be identified with acute multiple sclerosis. So long as the etiologic factors of the two diseases remain unknown, the nosologic separation will remain unsatisfactory and uncertain. It is not even known that the many cases diagnosed today as multiple sclerosis possess a common nosology.

#### SYMPTOMATOLOGY OF DISEASES OF THE RIGHT TEMPORAL LOBE. ALFRED HAUPTMANN, Halle, Germany.

The lack of characteristic symptoms in conditions affecting the right temporal lobe prompted Hauptmann to report the following case:

A girl, aged 20, had suffered since the age of 8 years from attacks in which she gazed into space or at a fixed object. The loss of consciousness during an

attack lasted but a minute; objects held in the hand were not dropped. Just before an attack she would experience a peculiar sensation and at times could control an attack by voluntary efforts. After an attack she remained tired and sleepy for about an hour. At the onset, there was macropsia with some of the attacks; objects appeared very large and seemed to move toward her. Under such conditions she experienced a peculiar change in consciousness, which can be described as *déjà vu*. It seemed to her that everything had already existed, and as if she knew what was going to happen. At first the attacks would come on five or six times a day; in the last three years they had come more frequently.

At the age of 19 there was pain in the right eye. It was thought to be a trigeminal neuralgia, and an injection was made into the first branch, with some relief from the pain. A roentgenogram of the skull at that time showed nothing of importance; the fundi were normal. Four months later, diplopia from paresis of the right abducens muscle, double choked disks, nystagmus, left hemianopia and occasional noise in the right ear appeared.

A little later, neurologic examination disclosed sluggish pupillary reaction to light and choked disks (right, 3 or 4 diopters; left, 4 or 5 diopters); the blind spot was enlarged on both sides; the visual field on the left was contracted for white and for colors; on the left, the scotoma for white was limited to the upper quadrants, while on the right it was in the lower quadrant. There was a right abducens paresis; the left abducens was slightly weak. There was a slight horizontal nystagmus. Sensation for touch and pain was diminished over the right side of the face; the right corneal reflex was diminished, and there was a slight right facial paresis. Taste and smell were not disturbed. There were no motor disturbances, no sensory disturbances of the trunk and the extremities and no cerebellar disturbances. Roentgen examination of the skull showed an increase in the *impressiones digitatae*, especially in the frontal and occipital areas. The sella showed the effect of increased pressure. The petrous portion of the right temporal bone was less dense than that of the left.

In summary: The attacks were of short duration, with loss of consciousness resembling that of petit mal, but with no convulsions. A definite diagnosis at that time was not possible. The fact that there was no response to antiepileptic treatment made the diagnosis of epilepsy doubtful. During some attacks there were macropsia and a feeling of *déjà vu*. Eleven years later, other acute symptoms appeared which pointed more to a localized process. They were: involvement of the right trigeminal nerve, choked disks, a mild left hemianopia, right abducens and facial paresis, right acoustic involvement, slight nystagmus and osseous disturbances at the base of the skull.

The newly developed symptoms pointed to a lesion at the base on the right side, most probably an angioma. A tumor of the cerebellopontile angle could be discounted by the absence of cerebellar symptoms. But the left hemianopia was against such a diagnosis; a tumor in this location could not explain this symptom. A trephine opening was made over the cerebellum; the patient died soon afterward.

Postmortem examination disclosed a soft, bloody tumor in the right temporal lobe. The right side of the pons was the smaller. Microscopically, the tumor was a dense, fibrous glioma, with a large number of monster glia cells. Could the diagnosis have been made from the symptomatology?

Cushing, in 39 cases of tumor in the temporal lobe, found hemianopia missing in 6 cases only. Kolodny, in 38 cases, found no hemianopic defects. Again, hemianopia may be brought about by a basal tumor exerting pressure on the optic radiations or on the lateral geniculate bodies.

The characteristic oculomotor paralysis in tumors of the temporal lobe was not present in this case. The abducens paresis was of no help in localizing the lesion; the same may be said regarding the involvement of the trigeminal nerve. Facial involvement in these tumors is usually contralateral. The absence of paresis of the extremities, together with involvement of several cranial nerves, pointed rather to a basal condition. Schwabach's test gave negative results in

this case. The roentgenologic changes in the bone were more in line with a diagnosis of a basal tumor.

As for the epileptiform attacks that were present for eleven years before the acute symptoms set in, they are more significant in the differential diagnosis, although epileptic attacks in tumors of the temporal lobe are rather of the convulsive type. Astwazaturow, among 43 cases, found 22 in which there occurred epileptic attacks. This is contradicted by others. According to Astwazaturow, epileptic attacks occur mainly with tumors of the right temporal lobe. To be sure, epileptic attacks occur with tumors in other regions in the brain, so that their presence alone does not prove location in the temporal lobe. But the attacks in this case were combined with the manifestations of macropsia and *déjà vu*. Even these two symptoms may be found in other conditions, such as neurasthenia. Attempts should be made to localize function in particular areas of the brain, without disregarding the unity of function of the central nervous system.

Jackson and Stewart described the so-called uncinæ fits occurring with tumors of the temporal lobe. At times there occurs a "dreamy state," during which surrounding objects appear unreal and distant, and at the same time "familiar," as if everything present had been there before, a *déjà vu*. Herpin described this condition as an intellectual aura, as a state during which the patient hears, sees and performs proper movements, without knowing what he hears, sees or does. The objects appear to be some distance away. A condition of double consciousness also appears. Apparently these conditions bear a close similarity to those observed in the case under discussion, except that in this case macropsia instead of micropsia was present. The temporal lobe is close to the optic radiation. Is it not possible that involvement of the temporal lobe, and perhaps especially of the right temporal lobe, may bring about a change in the optic conception? This would be in agreement with Pötzl's new conception of the influence of "neighboring spheres."

The same statement is true for the *déjà vu*. On the causes of this phenomenon opinions differ. Some consider it an expression of a local disturbance. In the case under discussion, it is to be assigned to a cerebral process of circumscribed type.

Typical uncinæ attacks were not observed in this case. Perhaps they depend on the localization of the tumor within the temporal lobe itself. Attempts have already been made to correlate the epileptic attacks with tumor in definite parts of the temporal lobe. So far this has not proved successful. No attempt has yet been made to correlate the accompanying symptoms that have been described with disturbances of definite parts of the temporal lobe.

In reviewing the symptoms in this case and their diagnostic application in pathologic conditions of the right temporal lobe, Hauptmann stresses the following points: The symptoms of tumor were preceded by attacks of petit mal for over eleven years. From the histologic observations it is reasonable to assume that intracranial pressure remained absent for some time. The symptoms of macropsia and *déjà vu* apparently are to be considered as characteristic in lesions of the temporal lobe. In cases of tumor of the temporal lobe the roentgenologic changes in the petrous portion of the temporal bone may be caused by pressure.

It is also to be noted that the growth and development of a tumor of the brain may extend over many years. This is of special interest in the question of the traumatic origin of tumors of the brain and the possible length of time of their development.

SOME METHODS OF INVESTIGATING THE FUNCTIONAL ABILITY OF THE VEGETATIVE NERVOUS SYSTEM, WITH SPECIAL REFERENCE TO THE VASCULAR SYSTEM. KATE HERMANN, Hamburg, Germany.

The object of this investigation was to learn more about the so-called vasoneuroses and kindred ailments. The study included well persons as controls. The following factors were measured: (1) blood pressure; (2) capillary reaction of the skin; (3) surface temperature; (4) volume of the extremities, and (5) sweating.

1. The blood pressure was taken after about a half hour of rest. Records were made with and without preceding stimulation by heat and cold. 2. About

10 cc. of ice was applied to the chest and to the upper and lower parts of the arms; observations included the time required (a) to change the color of the skin and (b) to change it to brick red. 3. In measuring the surface temperature, Dannmeyer's mercury thermometer was used. 4. Plethysmography was unsuccessful owing to a lack of proper instruments. 5. Sweating was tested only in patients; pilocarpine, acetylsalicylic acid and lime-tree flower tea were used.

In addition, in patients, the Aschner-Tschermak sign, the respiration, arrhythmia of the pulse and dermatographia were studied.

In a recent work on blood vessels of the skin, Lewis found that the reaction comes chiefly from the arterioles, capillaries, collecting veins and subpapillary venous plexus. These vessels are to be distinguished from the large arterioles which possess a strong musculature. Scratching the skin produces a slight injury of the tissue. This and the quantitative changes produce the white reaction and the typical triple reaction: local reddening, red halo and local edema. Experiments with heat and cold prove that the reactions obtained up to the point of the red halo depend on active dilatation or an increase in flow in the small blood vessels. These reactions are sharply limited to the injured tissue. The red halo depends on an active dilatation of the large arterioles as a local nerve reflex.

Lewis obtained these reactions regularly after applying various kinds of stimuli, both physical and chemical, and concluded that they are the result of setting free a histamine-like substance, although so far this has not been proved chemically. The most important fact is that all the reactions, with the exception of the red halo, do not depend on the nervous system; they are obtained when the peripheral nerve is sectioned, in lesions of the central nervous system and in sympathectomized vascular areas.

*Blood Pressure.*—Herman made observations of the blood pressure in 10 well persons without applying stimuli. Each observation lasted for twenty minutes, with an interval of two minutes. No change in the blood pressure was established. Twenty-five curves were plotted for 17 well or indifferent convalescent patients. The blood pressure was observed for forty minutes with an interval of two minutes. Heat and cold were applied and observations made. In 10 cases the curves were alike: Stimulation with heat brought about a slight lowering and stimulation with cold a considerable heightening of the blood pressure. The duration of the change effected was from five to eight minutes. In 7 cases the change in either direction lasted only one minute. In 5 of the 7 cases, the application of heat was felt as pain; in the 2 other cases, a high temperature (50 to 54 C. [122 to 129.2 F.]) was felt as just hot. Of the other eight curves five showed waves due to the application of heat and cold, but even without stimulation the curves showed irregularity.

Twenty-five curves were made for 13 patients with vegetative disturbances; all showed a much greater oscillation. In these cases, there seems to be not only a disturbed lability but also a disturbed stability; once an upset is induced, a longer time is required for the blood pressure curve to regain the former state of rest. Some of the curves showed greater stability, and some far greater oscillation. Some curves did not respond to heat and cold when the affected arm with sensory innervation intact was stimulated, while when the well arm or well leg of the same patient was stimulated, there were many oscillations.

The curves showed that in most cases, on stimulation, there is a change from the normal. In most cases there are a delayed response to the stimulus and a delayed return.

*Capillary Reaction of the Skin.*—Kestner's table shows that the average time for the appearance of the red brick color in well persons, after a piece of ice has been applied for three seconds, is eleven seconds; in sick children, it reaches eighty seconds; in 50 per cent of the cases, Kestner obtained no reaction. In 10 patients with vegetative disturbances Hermann found that the average time was at least six seconds. In 1 case, when the test was made over the chest, the reaction took twelve seconds, while in the same patient, when ice was applied to the legs, there was no reaction.

*Skin Temperature.*—These tests gave entirely negative results.

*Plethysmographic Studies.*—These yielded no results of importance.

*Sweat Reaction.*—The results are of interest, although no definite conclusion can be drawn. In carrying on this type of experiment, Hermann compared, in the same patient, the result obtained on the well part of the body with that obtained on the affected part. This was made necessary by the fact that there is no definite report of the sweat reaction in well people, that there is always a difference in the intensity, and that the type of sweating as a reaction to various mediums has not as yet been described. Hermann realizes that comparison between the result obtained on the well with that on the affected side is not entirely satisfactory, since one cannot be certain that some disturbance may not be present on the well side until normal sweat reactions have been established from a large number of studies.

In many cases Hermann found hyperhidrosis; the psychic nature of this was recognized from the fact that it occurred on one occasion, while during further examinations the same patient showed only very mild sweating. In 1 case, hyperhidrosis appeared only in the ears, which were extremely red. In 1 case an anhidrosis appeared in the affected hand.

In 1 case of fracture of the right alveolar process with dislocation of the left temporomaxillary joint, the patient complained of a lack of sweating on the left side of the face, while otherwise he sweated a great deal. On eating anything sour there also developed sweating on the left side of the face. When he was tested with acetylsalicylic acid and lime-tree flower tea, there at first appeared definite sweating only on the right side of the forehead, in the right nasolabial fold and on the right upper lip; twenty minutes later there appeared mild sweating over the same areas on the left side. With pilocarpine there first developed mild sweating on both sides, with slightly more on the right; later the sweating became profuse on both sides, although there was always a slight difference noticeable between the sides. On the basis of the presence of a sharply limited hypesthesia, the author assumes an organic basis in this case, with functional disturbances.

Three other organic cases were instances of Raynaud's disease, in which sympathectomy had been performed. One patient, when tested with tea and acetylsalicylic acid, showed absence of sweating on the arm on which operation had been performed after pilocarpine, 0.01 Gm., had been injected; sweating appeared also in the fingers of the hand of that arm. The operation had been performed three months before. This experiment showed diminished secretion of sweat in the area of operation, namely, the right side of the face and neck, the upper part of the chest and in the back of the neck on the right, while over the forehead and in the axillae no difference was noted. Without pilocarpine, this patient could be made to sweat in the palm of the hand, in the inguinal region and in the axilla. In another patient, sweating over the face and neck and on the hand opposite to the side of operation could not be produced with tea and acetylsalicylic acid; on the hand on which operation had been performed sweating was produced only over the thenar eminence. With pilocarpine the sweating at first was lacking on the side of operation; then it appeared over the nasolabial fold, upper lip and neck, at first as a fine punctiform sweat, which later was the same as on the other side. The same observation was true with sweating of the hand, except that sweating here showed greater intensity. Another patient showed practically the same reactions.

In 6 other cases of vegetative disturbances, similar results were obtained.

Stimulated by the work of Lewis, Hermann examined well and sick people for the triple reaction. Wheal formation was obtained after severe scratching of the skin, but never after injections of histamine. In patients, the reaction was tested for over the skin of the upper part of the back and over the forearm. In 6 well persons, the triple reaction was obtained with very light scratching. In all cases, it required stronger scratching to produce edema over the forearm than it did over the back. As regards dermatography in sympathicotonia, according to the former findings, it was expected that local edema would readily appear in patients

with vegetative disturbances. Hermann's findings contradict this assumption. In fact, at times she was unable to produce a scratch-wheal over the chest or back with even very strong strokes, nor could she find a distinction between positive and negative, or between red and white dermography; she always found reddening which was not sharply demarcated.

In summary, the author finds: 1. Measuring the blood pressure can be of value only after typical normal curves have been established. 2. The capillary reaction of the skin is useful and shows differences in time between well persons and patients with vegetative disturbances—stimulation time, reaction time and return time. 3. The temperature of the skin has not proved to be of help. 4. Measure of the volume of the extremities has not proved satisfactory. 5. Experiments with sweating are of considerable interest. 6. The reactions of Lewis are of considerable value in the study of conditions of the vegetative nervous system.

After using various methods and finding a delayed reaction time for some functions of the vegetative nervous system, the author believes that she is justified in assuming that in patients with disturbances of this system it is not a question of vasolability (vegetative), but of a slowing, a certain stability of the vegetative nervous system.

#### APHASIA IN POLYGLOTS. E. HEGLER, Hamburg, Germany.

Many studies had been made on recovery from aphasia in patients speaking several languages. According to Pitres and Ribot, the language that the patient used most is often the only one that returns; at any rate use of it is first to return, and use of other languages remains more or less defective. Others have found that at times use of the mother tongue is more severely affected. Recently, Minkowski reported a case of aphasia in a Swiss-German, whose mother tongue, and the language which he used most, was Swiss-German. In recovering from a complete aphasia following a trauma to the head, at first there was a return of the "high German," and considerably later the Swiss-German dialect returned.

Hegler reports the case of a youth, aged 18, with endocarditis, whose mother tongue was French. He also learned the English language. He had been for six months in Germany, where he had learned to speak German with some accent. One day he complained of a severe headache, the pulse became rapid, the face turned pale, and he lost consciousness. This was followed by aphasia. The heart was enlarged, with a loud systolic murmur, chiefly at the apex. Neurologically, there was weakness in the right arm and leg; the abdominal reflexes were not quite clear on the right; there was a Babinski sign on the right, and the tendon reflexes were increased. In a few days the total aphasia began to show improvement. The patient understood what was said either in French or in German, but he was unable to answer. Eight days later, he answered all questions in a stereotyped German. "Kann nicht," he would say and at the same time point to his throat. The aphasia showed gradual improvement, but it was observed that he always answered in German when French was spoken to him. When one counted in French, "un, deux, trois," he promptly continued in German, "vier, fünf, sechs." He recognized all objects and gradually learned to write their French names, but could not speak them. To his brother, who spoke only French, he answered in German. The patient gradually learned to count in French from 1 to 10. In time he began to learn simple single French words, but he continued to come back to German. He later died from other complications.

The interesting fact in this case is that in recovering he began first to speak German, which he had learned only recently, and not French, his mother tongue. According to Hegler, the assumption is justified that since it was in a German milieu that the patient found himself surprised with the hemiplegia, it was instinctive for him in this situation to reestablish the German language as a means of readjustment to his surroundings. Minkowski said that instinctive necessities generally supersede the developmental historical temporal priority, so that in aphasia the language biologically most useful is first and most completely regained.

## THE GENETIC-FUNCTIONAL STUDY OF THE CEREBROSPINAL FLUID. VON KAFKA, Hamburg, Germany.

While not unmindful of the advance made in the study of the cerebrospinal fluid since the days of Quincke, who, in 1891, introduced lumbar puncture, von Kafka thinks that investigation of this subject must take a new turn; it must follow genetic-functional lines. When Boyd, in his book on the cerebrospinal fluid, made the statement that "it is in truth a mirror which reflects every change taking place in that system," and when Hauptmann, speaking on the same subject, remarked that all or some substances, either physiologically or pathologically, must pass through the cerebrospinal fluid before reaching the central nervous system, it became evident that there is need of other and more thorough studies of the changes taking place in the cerebrospinal fluid in order to determine whether the conceptions cited are to be accepted or not.

What is known of the genesis of pleocytosis? The discussion by O. Fischer and Merzbacher appears to decide that the spinal fluid cells are mainly histogenous. But the word indicates mainly that some cells still remain problematic. Identification of the fluid cells with those of the meninges and brain succeeds only partially. It is not known even why the normal fluid contains so few cells (the normal aqueous humor of the eye contains no lymphocytes; on the other hand, it contains endothelial and tissue cells); likewise their origin is unknown.

The albumin reaction of the cerebrospinal fluid, which is so essential for diagnosis, is still a problem for interpretation. In addition to the fact that the origin of the normal albumin is still unknown (C. Lange's conception that it comes from destroyed round cells is improbable), it also is not known how the albumin is regulated normally. Much suggests that the normal albumin in the fluid comes from the blood (normal permeability), and that it is regulated by the choroid plexus since normally the albumin is nearly always maintained at a constant and even level. Much more numerous are the problems of pathology: the source of albumin, the division into globulin and albumin, the individual fractions within the globulin group, and the eventual organ or disease specificity for albumin. The albumin may come from the blood, from diseased meninges, from the central nervous system or, according to F. K. Walter, from the efferent lymph of the central nervous system. These questions can be answered only after careful investigations. Most of the albumin reactions give only an approximate quantitative reading, without any indication as to the quality. The separation of globulin from albumin is a step forward. With its assistance one can distinguish between the spinal fluid from dementia paralytica, which shows a large increase in globulin while the albumin is often diminished, and the fluid from acute meningitis, in which both globulin and albumin are increased, though the albumin far outweighs the globulin. Thus, the albumin quotient is of considerable significance. Demme showed by means of this albumin quotient the transition of a reflex into a purulent meningitis. However, matters are not so simple. It has been shown that in dementia paralytica there is also an increase of globulin in the blood. The assumption that albumin is derived mainly from the blood and that globulin appears only in acute inflammation of the meninges is therefore not entirely correct. In dementia paralytica globulin perhaps comes also from the blood. Von Kafka experimented to determine whether the albumin of the blood and that of the spinal fluid are biologically similar. He precipitated albumin from spinal fluid and albumin from serum, and performed precipitation experiments with spinal fluid and serum in different diseases. The experiments are not completed. They show, however, many differences in the relation between serum albumin and spinal fluid albumin, so that one cannot speak of a specific organ identity.

On the other hand, colloidal chemical experiments have shown differences in the globulin of the cerebrospinal fluid in different diseases of the central nervous system which cannot be referred to the globulin fractions. The globulin fraction in the cerebrospinal fluid offers a field for investigation. Von Kafka showed that in acute meningitis the precipitation of globulin begins to take place with an ammonium sulphate concentration of 28 per cent, in dementia paralytica with one

of 33 per cent and in chronic cerebral syphilis with one of 40 per cent, while normally the precipitation takes place with one of 50 per cent. Therefore, normally there is present in the fluid only residual globulin; in chronic cerebral syphilis, pseudoglobulin; in dementia paralytica, also euglobulin; in acute meningitis, also fibrinoglobulin. These relations are not known in serum, either normal or pathologic. Later, von Kafka and Samson showed that the euglobulin fraction does not occur in normal cerebrospinal fluid, and that traces of it are present in non-syphilitic organic diseases of the central nervous system, while in syphilitic diseases of the central nervous system the cerebrospinal fluid contains considerable euglobulin, the largest quantity being found in dementia paralytica and in acute non-syphilitic meningitis. If the ratio of euglobulin to globulin is taken, it is found that the euglobulin takes the higher figure in dementia paralytica.

Regarding the source of the Wassermann reaction in the cerebrospinal fluid, the following opinions may be mentioned: 1. C. Lange thinks that the Wassermann reaction in the fluid is formed locally only in dementia paralytica; in other conditions it is an unimportant phenomenon of permeability. 2. F. K. Walter is of the opinion that the reaction in the fluid is always locally formed (even in cases of acute meningitis with a positive Wassermann reaction of the blood). 3. According to F. Plaut, the reaction in dementia paralytica is not entirely formed locally, but comes also from other sources.

All investigators therefore agree that a positive Wassermann reaction in the cerebrospinal fluid can be produced locally, an opinion which Wassermann himself expressed with reference to the spinal fluid and also to the aqueous humor of the eye. This opinion, however, overlooks the fact that it attributes to the spinal fluid a marked ability to produce antibodies. The investigation by Plaut and Grabow on recurrent infections shows that the formation of antibodies in the subarachnoid space takes place with difficulty, that it is very weak and does not account for the formation of antibodies in the serum. It is therefore necessary to explain the Wassermann reaction in the fluid, or a part of it, in some other way. In agreement with this opinion appears to be the observation by von Kafka and Gozzano that the substance bringing about the Wassermann reaction can be removed from the fluid by shaking it with ether, and that this substance can be extracted from the ether. Nor is the Wassermann reaction in the cerebrospinal fluid absolutely dependent on an increase of globulin. The Wassermann reaction may be present without an increase in the globulin. The Wassermann reaction apparently stands in close connection with pathologic metabolic changes of the central nervous system. A part of the Wassermann reaction in the fluid probably comes from the blood.

Genetic-functional study of the cerebrospinal fluid, according to von Kafka, requires: (1) not only recording spinal fluid phenomena, but careful thinking along theoretical lines followed by experiment; (2) many investigations of the spinal fluid along practical lines; (3) analysis of observations on the cerebrospinal fluid with reference to individual components. Investigation of the cerebrospinal fluid should be carried on even when diagnostically there seems to be no need for it. A carefully investigated fluid may bring new discoveries and often may be worth more than a large tabulation of statistics.

SIGNIFICANCE OF THE INCREASE OF ALBUMIN WITHOUT A CORRESPONDING INCREASE OF CELLS IN THE SPINAL FLUID. AXEL W. NEEL, Copenhagen, Denmark.

Froin's syndrome, reported in 1903, includes a yellow color and spontaneous coagulation. In Froin's first 3 cases there was also a lymphocytosis; these were cases of syphilis with occlusion of the subarachnoid space. Similar cases were reported in the same year by Babinski and by Cestan and Ravaut. In 1905, Donath reported a case of Landry's paralysis with xanthochromia and coagulation of the fluid. Similar cases were reported by others. In 1909, Blanchetière and Lejonne reported a case of tumor of the spinal cord with Froin's syndrome. In 1908 and 1910, Nonne reported 6 cases of tumor of the spinal cord; the globulin reaction was marked (marked phase I), but the cells were few. Soon afterward similar cases were reported by many other investigators. This combination of a strong phase I

reaction with few cells is referred to in the German literature as Nonne's compression syndrome; at times a yellowish discoloration of the fluid may also be present in these cases.

Cases of Froin's syndrome as originally described by Froin are relatively few (as a rule most cases do not show lymphocytosis). To this group were therefore also added cases characterized by a large increase of the albumin with very few cells, which the French call *dissociation albumino-cytologique*. Nonne's compression syndrome similarly depends on such a compression, but at the same time there are other causes for the combination of few or no cells with an increase in albumin, so that compression cannot be blamed in all cases. None the less, when a spinal fluid shows an increase in albumin without a corresponding increase in cells the possibility of compression comes to mind. Such a dissociation occurs in many different diseases of the central nervous system, especially when cases are included in which the increase in albumin is relatively small (to about 15 mg. per hundred cubic centimeters). In cases in which the increase in albumin is comparatively higher (above 15 mg.), compression is a more frequent cause. In inflammatory conditions, for example, in dementia paralytica, there is often a considerable increase in albumin without an increase in cells. A similar condition may at times be observed in chronic epidemic encephalitis or in late syphilis with

TABLE 1.—Amount of Total Albumin in the Spinal Fluid in Various Diseases

Disease	Total Albumin, Mg. per 100 Ce.		
	Under 20	20 to 100	100 to 1,000
Intraspinal tumor.....	1	6	8
Vertebral tumor and metastasis.....	11	4	10
Spondylitis tuberculosa.....	..	3	6
Posttraumatic disease.....	..	6	4
Arachnoiditis cystica.....	..	..	2
Syphilis.....	..	..	7
Tuberculosis.....	..	..	3
Encephalitis.....	..	2	3
Cerebral hemorrhage.....	..	16	7
Polyradiculitis.....	2	12	6
Monoradiculitis.....	..	6	..
Doubtful.....	1	2	..
Tumor of the brain.....	134	53	..
Sciatica.....	88	1	..

encephalomalacia. In some cases it is not apparently the result of arteriosclerosis. It should be noted, however, that the cell count is not normal, but is merely low.

Table 1 shows the amount of total albumin in the spinal fluid in various diseases.

Neel found spontaneous coagulation only in cases of compression, that is, in cases of intraspinal tumor, tumor or inflammation of the body of the vertebra, syphilitic diseases and 2 cases of cystic arachnoiditis. In these cases the albumin averaged 540 mg. per hundred cubic centimeters. In most cases the disease affected the lumbar or lower dorsal area. Compression in the upper part of the canal may also bring about coagulation of the fluid, depending on the degree of closure of the spinal canal. According to Sicard and Descamps, coagulation is caused by pressure on the veins below the block, from which blood plasma with fibrinogen and fibrin ferment exudes into the spinal fluid. If inflammation is present, inflammatory products are added. In rare cases coagulation may be the result of an artificial mixture with blood as a result of the lumbar puncture. This will occur in cases in which the albumin in the fluid is greatly increased and contains a little fibrinogen, the addition of the blood caused by the puncture being sufficient to bring about coagulation.

Neel calls attention to the possible dangers of lumbar puncture and to the usefulness in certain cases of a second puncture, usually suboccipital. The fluid below the point of compression often contains a large increase of albumin, while the fluid above the compression contains comparatively little. Likewise, the author stresses the importance of the Queckenstedt test in this type of case. Injection of iodized oil may cause unpleasant results.

In group 1 of the table, in a case showing a small increase of albumin Neel found post mortem a neurinoma, the size of a hazelnut, coming from the posterior root of the atlas. In another case there was a large intramedullary melanosarcoma embracing the lower part of the pons, the medulla and the upper part of the cord. It was difficult to understand how a tumor of this size could have developed. Another case in the group was that of a woman, aged 30, who was successfully operated on for an extramedullary tumor. After a pregnancy extramedullary symptoms again developed. Apparently the pregnancy aggravated the condition. There was 1 case of syringomyelia with local gliosis which brought about a compression. Among those with a large increase of albumin was 1 case of an aneurysm, the size of a plum, situated at the cauda. This case showed a complete Froin syndrome with albumin increased to over 1,000 mg. per hundred cubic centimeters.

In the second group were mainly cases of metastatic tumors involving the vertebral bodies and meninges. In 1 case the first lumbar puncture gave globulin 1 mg. and albumin 15 mg. per hundred cubic centimeters. Two months later, a second lumbar puncture gave globulin 30 mg. and albumin 300 mg. In patients with symptoms of stiffness in the back and radicular changes a lumbar puncture often reveals the nature of the disturbance. In some cases roentgen treatment may be advisable. One case was that of a plasmocytoma in the dorsal part. This resulted in a progressive polyneuritis with complete muscular atrophy. This tumor embraced the largest part of the bodies of the first and second dorsal vertebrae and surrounded the dura. The myelin sheaths of the peripheral nerves of the lower extremities, and to a lesser extent of the upper extremities, were entirely lost. In the medulla, Marchi degeneration was present in the posterior column. Two cases of lymphosarcoma and myelosarcoma presented symptoms like those of Landry's paralysis.

In the fourth group, the trauma often was caused by a sudden turn of the body in lifting or carrying a heavy load. Many cases occurred during the war. The process is apparently an arachnoiditis with cyst formation. The traumatic lesions in the cord consist mainly of necrosis; a lesser number, of hematomyelia. Such conditions may develop after mild traumas.

Groups 6, 7 and 8 were cases of inflammatory conditions (syphilis, tuberculosis) or an indefinite combination of inflammation and compression (encephalitis). The increase of albumin in the cases of syphilis and tuberculosis as a rule had its origin in a circumscribed meningeal process or in a localized inflammation. Encephalitis apparently tends to cause radicular manifestations, as some cases showed a flaccid paralysis, which in time improved and at times was followed by complete recovery. Similar cases of epidemic encephalitis have been described by many investigators. It should be noted that a combination of inflammation with compression changes in the spinal fluid has also been described in acute meningitis.

In group 9, the increase in albumin does not depend on a local arachnoid block; therefore, the Queckenstedt symptom is absent. The cases are mainly those of cerebral hemorrhage; most of them are in old persons in whom paralysis suddenly develops. Post mortem, hemorrhages are found in the corresponding area. In some cases the spinal fluid was clear; in others it was yellowish or contained blood.

The cases in group 10 showed a flaccid paralysis of varied degree. Four cases with a slight increase of albumin were cases of diphtheria. In other cases the etiologic factor remained uncertain. In 1 case pregnancy was the only observable cause. In very marked cases the symptoms were those of a typical Landry paralysis, with rapid development of the paralysis, accompanied by paresthesia, indicating that the sensory nerves were also involved. In these cases the increase of albumin was as high as from 250 to 300 mg. or more per hundred cubic centimeters.

In group 11, 5 cases presented symptoms similar to sciatica, except that the pain spread over a larger area and was not limited strictly to the sciatic nerve. In 1 case the symptoms were limited to the arms. In a few cases epidemic encephalitis appears to have been the causative factor. One was most likely a case of poliomyelitis.

Group 12 has no particular designation. One case with a subacute course presented a progressive paralysis, without involvement of the deep reflexes, and later coma and death. Post mortem, the anterior horn cells were involved; there were hyperemia and rupture of some blood vessels and splitting and edema of the roots. Another case of coagulation of the spinal fluid, with 1 cell, globulin 4 mg. and total albumin 50 mg., was complicated by a strongly positive Wassermann reaction of the blood, aneurysm of the aorta and multilocular cysts of the kidneys. The patient had convulsions. Post mortem, there were softening of the brain and a cyst; in the cord there were hyperemia and degeneration of the anterior horn cells.

RECOGNITION OF GLIOMA OF THE SPINAL CORD WITH TERMINATION IN SYRINGOMYELIA. H. PETTE and St. KÖRNYEY, Magdeburg, Germany.

The authors present 2 cases of considerable interest as bearing on the question of syringomyelia.

CASE 1.—A man, aged 45, in 1924, fell with a heavy weight from a steep place, striking the back of his head and the entire back. For a short time he felt stiffness and tension in the left leg. A few months later sharp pain suddenly developed in the back of the neck, radiating to the shoulders and arms, more on the left than on the right side. This lasted for only a few days, but returned again in a few months. In August, 1926, a similar attack occurred, but this time there also appeared weakness in both legs. A few weeks later, the mentality began to suffer; speech became indistinct; the left patellar reflex was much diminished, and there was diminished sensibility over the left side of the body. Two months later, a lumbar puncture revealed considerable increase in the pressure of the spinal fluid; the fluid was brownish yellow and somewhat turbid, and contained many cells, mostly lymphocytes; albumin was markedly increased, and the Wassermann reaction was negative. The condition of the patient gradually grew worse. In March, 1927, choked disk developed, more so in the left eye. A suboccipital puncture gave a clear fluid which showed no increase in the cells or albumin. In July, the choked disk increased; near the papilla were white areas (fatty degeneration); there was limitation of motion of the head forward; the sense of smell was diminished; there was slight paresis of the right facial nerve, and speech was bulbar in type. In walking the patient had to be assisted; there was some ataxia; motor power in the left hand was slightly diminished; there was no atrophy; the left leg was somewhat weaker than the right and showed atrophy; the dorsal and plantar reflexes were diminished on the left and only slightly diminished on the right; the right patellar reflex was diminished, and the left was absent; the achilles jerk was active on both sides; the abdominal reflexes were absent; the cremasteric reflexes were weak, and the anal reflex was not obtained. There was hypesthesia for all qualities in the outer, upper and inner side of the left leg.

In July, 1927, a lumbar puncture gave only 6 or 7 drops of a lemon-colored fluid; the Queckenstedt test was positive; albumin was strongly increased, and the cell count was  $2\frac{2}{3}$  per cubic millimeter, comprising lymphocytes only. The area of hypesthesia then included the entire left leg, but there was no dissociation of sensibility.

Six days later, a suboccipital puncture was done; 30 cc. of clear fluid was removed; it contained increased albumin with a cell count of  $\frac{8}{3}$ . In a few hours the psychic disturbance showed marked improvement. Even the physical symptoms showed improvement, and speech became clear. In the latter part of August, the symptoms again became aggravated; the patient complained of severe headaches; consciousness was clouded, and he had hallucinations. This condition lasted for a few days, and then suddenly all symptoms cleared up. The patient said that he experienced a sudden push, "as if a membrane had broken and a fluid had run downward from above." At the end of September, he again complained of headaches and showed psychic disturbances, which disappeared in a few days. In October, he again had headaches, pain in the left side of the face and paresthesias in both arms. The sensory disturbance showed some dissociation. There was an increase in the ataxia of the legs. In January, 1928, vision and hearing

became further impaired; there was a constant noise in the ears; speech became more indistinct; weakness in the lower extremities became more marked; the right patellar reflex disappeared, while the achilles reflex remained, and the sensory disturbance was present as before.

On January 23, trephining was done over the right temporal lobe. The brain was under considerable pressure; 60 cc. of fluid was removed from the lateral ventricle. In spite of a temporary improvement in the general condition, the vision became poorer.

On February 14, the posterior fossa was opened. After removal of the arch of the atlas, the dura was found to be under considerable tension. At the entrance to the fourth ventricle was a small cyst containing clear fluid; the meninges around it were somewhat thickened. The patient died on the following day.

Post mortem, the meninges of the brain were cloudy, especially at the base. In the prepuduncular area the meninges were thickened, especially near the chiasm. The optic nerves, especially the left, were embedded in the membrane. Near the medulla the membrane again became thickened; the thickening reached to the cerebellum and involved the eighth, ninth and twelfth cranial nerves. At the temporal poles there were hard yellowish tumor masses. In the cord the dural sac at the cauda was enlarged and thickened; above it was in places attached to the leptomeninges. The leptomeninges were thickened in places, more over the posterior than over the anterior surface. The conus and filum terminale were very thick, and the roots were covered with a thick, fibrous tissue. At the first right sacral root was a nodular mass. On cross-section the center of the lower part of the sacral cord was reddish; oralward it increased in size and was recognized as a necrotic tumor mass. This tumor in the area of the fifth lumbar and twelfth thoracic segments took in the greater part of the cross-section of the cord. It was surrounded by a border of displaced cord substance. In the lumbar area the cord was enlarged, and with Weigert's stain it was found to be distorted by the tumor mass.

The tumor consisted of masses of small round nuclei embedded in a homogeneous ground substance. The nuclei were somewhat larger than normal small dark glia nuclei. They were rich in chromatin. In addition, there were also larger nuclei of a lighter color, with irregular as well as double nuclear elements. Many of the cells had no protoplasm or very little, while some had a large protoplasmic body. There were large bodied cells with vacuolation. There were no cells of an epithelial character. Occasionally there were hemorrhages in the tumor tissue. The tumor was usually marked off from the surroundings by a glial ring in which monster glia cells were noted.

A cavity was found at the twelfth dorsal segment. The size and shape of the cavity varied in different segments. In the lower dorsal segments it dented the gray commissure; in the upper dorsal and cervical segments there was a break in the posterior horns. The cavity was surrounded by glia characteristic of syringomyelia, and was distinct in outline from the cord substance. No epithelial lining was noted in the cavity. In the anterior border of the gliosis were many degenerated nerve fibers. In the wall of the cavity were some degenerated areas, and old and fresh hemorrhages were present. At some levels the central canal could not be made out; at other levels there were accumulations of ependymal cells.

In many cross-sections glioma cells were present in larger or smaller numbers in the gray substance; some showed necrosis. These groups everywhere were separated from the normal parenchyma. These cells were identical with the cells of the large tumor in the lumbar area.

At the lower border of the medulla, the meninges were considerably thickened and contained groups of tumor cells and occasionally single cells of this type. In the adjacent blood vessels, lymphocytes were frequent. At the crossing of the pyramidal tracts posteriorly, there were infiltrating tumor cells, brought by the blood vessels from the meninges into the white substance. These cells were elongated and had a larger cytoplasm.

Between the cerebellum and the medulla, in the hard collagenous substance of the pia, were large masses of tumor cells. A similar condition was present in the

meninges in the prepuduncular area, with the exception that in some places the connective tissue was even more firm. The cortical meninges appeared to be free.

Two distinct processes can be observed in this case; a tumor, with cavity formation, affecting considerable areas of the cord, and a diffuse tumor within the meninges of the cord and at the base of the brain. The character of the cells is the same in both processes. Apparently it is a case of metaplasia of derivatives from one and the same kind of cells of spongioblastic origin. The connective tissue formation is secondary, produced by irritation of the meninges by the glioma cells.

From the anatomic findings and the clinical course it appears that the origin of the tumor was intramedullary, and that later the growth spread to the meninges. How the tumor reached the periphery cannot be told from the histologic picture. There is no evidence to show that it reached there by continuity. The symptoms began with weakness in the left leg. The process therefore must have started in the lumbar region of the cord. The discrepancy between the comparatively mild disturbances of the legs and the high grade changes observed in the cord is only apparent. Histologically, everywhere in the cord there were a large number of well preserved motor cells. The tumor growth distorted, but did not destroy, the cord. The pain in the shoulders and neck indicates that the cervical cord became involved; since the pains were neuralgic, it must be assumed that the growth was extramedullary radicular. This is supported by the anatomic demonstration of a tumor-like thickening of the meninges of the cervical cord, in which some posterior roots were embedded. The periodic headaches and mental disturbances can be explained by the assumption that the path of the cerebrospinal fluid was periodically blocked by obstruction of the fluid as it entered the cord. This is indicated by the lumbar fluid showing the compression syndrome while the cisternal fluid was normal. The sudden onset of headaches and mental disturbances and their sudden disappearance indicate a disturbance of the flow of the cerebrospinal fluid within the cranium. Anatomically, there was a massive accumulation of tumor elements between the medulla and the cerebellum. A similar explanation is found for the disturbance of taste, the facial paresis and the bulbar manifestations. The choked disk was the result of an involvement of the chiasm. The clinical symptoms are therefore explained by the anatomic findings.

Of special interest is the diffuse distribution of the gliomatous process within the meninges, which is rare when compared with sarcomatous and carcinomatous diffusions. In 2 of Löwenberg's cases the infiltration took origin from the brain.

All investigators stress the point of the morphologic changes of the tumor in different areas. In this case, too, changes were observed in the different cell groups. The neoplasm in the cord showed differences from that observed in many of the meshes of the subarachnoid space. In the medulla the process was different, while in the region of the chiasm the cells were similar to those observed in the meninges of the cord. Apparently the variability of the cell elements depends on the soil in which they multiply. In this respect it appears that the spinal cord tissue offers conditions different from those of the pia. The metaplasia therefore depends, on the one hand, on the character of the cells and, on the other, considerably on the tissue on which the tumor grows.

With some differences in the growth of the tumor, the distribution is the same as in diffuse sarcoma and carcinoma. Diffusion occurs through the cerebrospinal fluid and the lymph. It is similar to acute and chronic inflammation of the meninges. On the basis of experimental work and human pathology, Pette had previously established that this condition is true for all meningeal tumors, and that there is practically no difference between the sarcomatous or carcinomatous type and the gliomatous type. What difference there may be is due to mechanical factors which depend on the circulation of the cerebrospinal fluid and the fact also that in gliomas more lesions are present in the meninges and the connective tissue in places is considerably thickened.

Corresponding to the relatively slower growth of the glioma as compared with carcinoma and sarcoma, the duration of the illness in diffuse glioma is longer. In the case reported the illness lasted three and one-half years. It is also well to

note that the disease in this case developed at the age of 40; in most other cases reported in the literature the disease affected younger persons.

Symptomatically, there are some differences between the two types of diseases. In the sarcoma-carcinoma type, on account of the more even and greater distribution and the more rapid growth, the symptoms appear earlier and are more varied than in glioma. Hence in glioma a diagnosis cannot be made in the early stage. In 1921, Pette proposed a symptom-triad for the diagnosis of diffuse meningeal carcinoma: (1) symptoms of meningeal irritation (epileptic attacks, psychic anomalies and stiffness of the neck); (2) involvement of cranial nerves (visual, auditory, facial and oculomotor), and involvement of spinal roots (loss of deep reflexes; paresis); (3) tumor cells in the spinal fluid, with marked increase in albumin. A similar condition may be observed in sarcoma of the meninges. In diffuse glioma the increase of albumin in the spinal fluid appears to be constant. Tumor cells have so far not been found in the fluid, a fact which is explained by the peculiar histologic processes. Involvement of the cranial nerve was repeatedly observed, as in this case.

The diagnosis in this case could have been made on the following findings. There were atrophy of the legs, dissociation of sensibility and reflex anomalies, all of which speak for an intramedullary process; for the meningeal involvement speak the root symptoms, involvement of the basal cranial nerves and the choked disks. These symptoms appear to be characteristic of a meningeal tumor, if it is assumed that the process was at first intramedullary and secondarily affected the meninges.

CASE 2.—A woman, aged 42, eight years before had had pain between the shoulder blades and a drawing and stiffness in the back of the neck. Five years later, weakness of the legs and sensory disturbance of the lower part of the body set in. Gradually the paralysis extended to the upper part of the body. There also developed bladder and bowel trouble. There was complete loss of sensation from the seventh cervical segment downward; between the third and sixth cervical segments there were dissociated disturbances. The lumbar fluid gave the typical compression syndrome, while cisternal puncture gave a normal fluid. The diagnosis pointed to an involvement of the upper part of the cord, but it could not be decided whether it was intramedullary or extramedullary. The patient died suddenly of paralysis of the heart.

Post mortem, a tumor mass was found embracing nearly the entire cord. In the cervical and upper dorsal regions the tumor was sharply outlined against the cord tissue, and apparently was of central origin. It crowded out the cord so that only a small border remained. Near the medulla was a cyst, which did not communicate with the ventricle, but blocked the approach to the posterior fossa and was connected with the cavity of the medulla and of the upper cervical cord. At the level of the fourth thoracic segment, in addition to the tumor, there was a cavity surrounded by glial tissue similar to syringomyelia. The tumor sharply disappeared at the fourth thoracic segment, and only the cavity remained; it had its largest expansion at the fourth lumbar segment, and reached down to the conus terminalis. Beginning with the fourth thoracic segment the glial border began to thin out, and in places disappeared entirely. Above the tumor mass, in the region of the medulla, was another cavity, which was also surrounded by a glial border. This cavity reached up to the lower border of the inferior olive. The tumor consisted of cells of epithelial type grouped around the blood vessels; some were cylindriciform, like ependymal cells; others were of cuboid shape.

The clinical symptoms are explained by the anatomic findings. Tumors of the cord similar in character have been reported by many observers. W. Rosenthal named the condition neuro-epithelioma gliomatousum microcysticum. With the Golgi stain he was able to show that the processes from the cylindric cell bodies of the tumor tissue showed ramifications like those of embryonic ependymal cells, or spongioblasts. Bittorff's case resembled in many ways case 2. In his case the tumor was surrounded by a gliosis, and contained small cavities lined with cells transitional from cuboid to cylindric epithelial cells. Marburg described a similar tumor under the name blastoma ependymale. Similar cases were described

by Forster and Ostertag, and by Kirch. Bailey and Cushing described this type of tumor under the name of neuro-epithelioma, and considered the tumor cells as primitive spongioblasts; they are characterized by their rosette formation, and are present in small cavities.

Concerning the pathogenesis of syringomyelia, Schieffendecker and Leschke, Henneberg, Bielschowsky and Unger and Ostertag believed that it is caused by dysontogenetic factors. Kirch maintained that a distinction should be made between intrablastomatous and extrablastomatous cavities. He believed that fundamentally syringomyelia is similar to cavity formation in the brain "in so far as they both develop from any kind of blastoma." In one group the cavity is formed by the breaking up of centrally lying tumor tissue, so that the inner wall of the cavity is composed of remains of tumor tissue. From this group Kirch separated others that are more common from syringomyelia in that they are supposed to develop as a result of a circulatory disturbance which causes a serous transudation in the tissue around the tumor. In this way there is gradually formed, besides the tumor, an encapsulated glial cavity filled with fluid.

Without discussing the merits of Kirch's opinion, the general conception of syringomyelia today is that it is a disease which pathogenetically is closely associated with ectodermal processes and their later development. Regressive changes with cavity formation may be found in other conditions, such as in sarcomas and carcinomas, but no one would classify these with syringomyelia. Pette and Környey, however, are of the opinion that syringomyelia is not a nosologic entity, not even when the disease is limited to purely gliomatous types, but that rather different cases may be of different origin. From the findings in the cases reported the authors conclude that the cavity is formed by the breaking up of tumor tissue as a result of necrosis, and that the surrounding layer of glia represents a reaction of the functionally damaged cord to the tumor. Pette and Környey were unable to substantiate the conception of Bielschowsky and Unger and Creutzfeldt that it is to be considered as of spongioblastic origin from the tissues remaining attached to the wall, and that the glial border has a blastomatous character. The authors believe it to be of secondary origin, as a reaction to the damaged cord tissue.

How much influence the pressure of the growing tumor and the biologic chemical processes have on the development of the glial wall cannot be stated. That foreign cell elements exert a strong irritation on ectoderm and even more on mesoderm is indicated by the intrameningeal tumor elements observed in case 1.

Regarding the importance of the connective tissue increase in the glial bands, Bielschowsky and Unger believed that the overgrowth of the connective tissue, regardless of whether it appears as membranes in a cavity wall, as solid balls, as meningeal rings or as a fibrosis of a vascular wall, is to be considered as a disturbance of embryonic development. Admitting this possibility in cases of connective tissue tumors, it does not warrant a generalization of this conception. Mesodermal tumor formations and connective tissue proliferation coming from vascular walls are qualitatively different processes.

From the observations mentioned it may be concluded that the cavity formation within the cord is the result of a breaking down of the tumor mass, and that the glial wall tends to mark off the tumor. The glial wall is not to be considered as a true blastoma. It should also be stated that not all forms of gliosis in syringomyelia develop in the same way. The importance of circulatory disturbances in connection with cavity and gliosis formation appears to be established. Gliosis and syringomyelia in extramedullary tumors can be explained in this way, especially when arachnoid cysts are present at the same time. In the interpretation of the genesis of cavities, the histologic findings offer a problem. Teratologic observations make it likely that abnormal formation of glia is originally present regardless of whether it is of blastomatous nature or not.

SIX YEARS OF MALARIA THERAPY IN DEMENTIA PARALYTICA IN THE LANDES-HEILANSTALT NIETLEBEN. B. PFEIFER and VON ROHDEN, Nietleben.

This article contains many charts and discusses treatment with malaria in great detail; much of it cannot be abstracted.

The authors report 300 cases in which the patients were treated with malaria in six years. In deciding on malarial treatment, the following factors were considered: the bodily condition of the patient, and the state and form of the dementia paralytica. Advanced and severe cases in which improvement was not expected were excluded, as were cachetic patients. Compensated cardiac disturbances and aortitis offered no contraindication to the treatment, provided the pulse and heart were watched during the fever; when necessary, the fever was stopped. Care is required in fat people. Old age is not a counterindication to treatment. Juvenile and senile forms generally showed mild remissions. But the authors frequently observed good results even in such cases. Of the 300 cases, 269 were in men and 31 in women; the ages ranged between 11 and 60; 126 were between 41 and 50. From 3 to 5 cc. of blood was injected, in most cases into the gluteal muscle; in a few the injection was given intravenously.

In most cases, after the injection of blood there develops an albumin or resorption fever, which often appears on the day of the injection or on the following day, and which ordinarily lasts from one to three days; occasionally it will last for from six to nine days. This fever is usually subfebrile.

The period of incubation depends largely on the kind of injection, the quantity of the parasites transmitted and the more or less favorable entrance into the blood stream. There is no doubt that receptability and resistance to the malaria play an important part. In intravenous injections the period of incubation is between three and eight days; in subcutaneous injections, from seven to twelve days, and in intramuscular injections, from ten to twenty days. It is important to note the height of the fever, the number of chills and the type of fever. It is often difficult to differentiate between the first malarial chill and the prodromal fever. At the height of the fever, the temperature fluctuates between 102 and 107 F.; the average is between 104 and 106 F. The number of chills necessary is usually accepted as from eight to ten; in special cases it may be increased to twelve. The purely tertian type is observed in very few cases. In some cases the fever suddenly disappears, remains absent for some time and then spontaneously reappears. There are types of fever which cannot be classed as a simple, double or mixed type. In 16 cases, after from two to eight chills the temperature dropped to normal and remained there. In 9 of these 16 patients it was found that on the average they had been treated with malaria a year before in another institution. One of the patients had had natural malaria. In the other patients no cause was found.

The subjective complaints during the malarial treatment are headaches, pain in the limbs, fatigue, loss of appetite and thirst. During the fever, and especially during the latter half period, the patients are slightly stuporous. Vomiting may take place; intestinal disturbances may be present; icterus occurs occasionally; anemia is frequent. The hemoglobin content drops to between 50 and 60 per cent during the fever, and there is a considerable loss of weight. Among the complications to be mentioned are cardiac and circulatory disturbances. Occasionally, vegetative disturbances appear suddenly, such as a rapid loss of weight and conditions of collapse. The fever was stopped when the systolic blood pressure went below 90. The period of incubation showed no difference between the first half of the patients treated and the second half (the 300 patients were inoculated with the same strain of malaria). The number of attacks of fever showed a slight decrease in the second half, which might indicate a diminution of virulence, but this is questionable. In addition to the duration of the disease, the age and the bodily type of the patient and the clinical course, the type of the course of fever to a certain extent has some influence on the cure. Definite relationships between the individual types of fever and recovery were not observed.

Discontinuation of the fever is brought about by giving 5 Gm. of quinine within seven days, 0.5 Gm. twice a day for the first three days. Injections of quinine were used when rapid action was required, as when complications took place. In nearly one half of the cases the temperature dropped to normal and remained there after the first dose of quinine. In a larger number of cases, after the first treatment with quinine one more chill occurred. After the fever was stopped by

means of quinine spontaneous relapses did not generally take place. In half of the cases the treatment was followed with an arsenical preparation.

A second course of malaria was undertaken in patients in whom the fever had had to be discontinued on account of weakness of the heart, and in 18 others in whom the cure failed to bring much result. The intervals between the treatments were between three and thirty months. During the second treatment the fever was much milder. In 16 of the 18 cases the fever stopped spontaneously, and

TABLE 3.—Results Obtained from Treatment

Result	Number			Percentage		
	Men	Women	Total	Men	Women	Total
1. Complete remission .....	29	1	30	10.8	3.3	10.0
2. Partial remission .....	131	23	154	48.7	74.2	51.3
(a) Ability to return to former vocation or one similar, but with diminished ability .....	33	5	38	12.3	16.1	12.7
(b) A lower grade of vocational ability .....	48	10	58	17.8	32.3	19.3
(c) No vocational ability, but capable of being discharged .....	30	6	36	11.2	19.4	12.0
(d) Not capable of being discharged, but capable of being employed .....	20	2	22	7.4	6.4	7.3
3. Unchanged .....	37	1	38	13.7	3.2	12.7
4. Aggravated symptoms .....	14	3	17	5.2	9.7	5.7
5. (a) Died of malaria .....	8	2	10	3.0	6.4	3.3
(b) Died of other causes .....	50	1	51	18.6	3.2	17.0
Total .....	269	31	300	100.0	100.2	100.0

TABLE 5.—Results of After-Treatment

Result	Malaria, 159 Cases			Malaria and Arsenical Preparation, 141 Cases			Malaria, Percentage			Malaria and Arsenical Preparation, Percentage	
	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female
1. Complete remission (cured) .....	10	1	11	19	8.0	3.2	6.9	13.5	13.5	13.5	13.5
2. Partial remission .....	52	23	75	79	40.6	74.2	47.2	56.0	56.0	56.0	56.0
(a) Ability to return to former vocation .....	15	5	20	18	11.7	16.0	12.6	12.8	12.8	12.8	12.8
(b) Vocational ability of lower grade .....	17	10	27	31	13.3	32.3	17.0	21.9	21.9	21.9	21.9
(c) No vocational ability, but sufficiently improved to be discharged .....	9	6	15	21	7.0	19.4	9.4	14.9	14.9	14.9	14.9
(d) Not capable of being discharged, but capable of being employed .....	11	2	13	9	8.6	6.5	8.2	6.4	6.4	6.4	6.4
3. Unchanged .....	17	1	18	20	13.3	3.2	11.3	14.2	14.2	14.2	14.2
4. Aggravated symptoms .....	7	3	10	7	5.4	9.7	6.3	5.0	5.0	5.0	5.0
5. (a) Died of malaria .....	8	2	10	..	6.2	6.5	6.3	..	..	..	..
(b) Died of other causes .....	34	1	35	16	26.5	3.2	22.0	17.3	17.3	17.3	17.3
Total .....	128	31	159	141	100.0	100.0	100.0	100.0	100.0	100.0	100.0

1 patient failed to react. In only 1 case was quinine required to stop the fever. The period of incubation was longer in this group of cases. This indicates that the first malarial treatment produces a relative immunity, which is still present after eleven months.

In 4 cases a third malarial treatment was undertaken. The interval between the second and the third treatment was, on the average, thirteen months. Three of the patients failed to react. One patient, after his temperature had risen twice, remained without chills. This case therefore presented a nearly complete immunity. Apparently a third malarial treatment is seldom of any therapeutic value.

In table 2 the authors give the results obtained in the 300 patients treated both with malaria alone and with malaria and an arsenical preparation.

As criteria for the degree of remission not only were the psychic and somatic findings taken into consideration, but above all the social usefulness. Serologic and even neurologic and intellectual improvement are less important than the ability to return to the former occupation and usefulness.

In table 5 it may be noted that the combined method of treatment brought a larger percentage of recoveries. The percentage of complete remissions with malarial treatment alone was 8, while with the combined treatment it was 13.5; the partial remissions also increased from 40.6 to 56 per cent.

**Catamnestic Results:** Reports from 143 patients of the total 162 discharged revealed that: the percentage of complete remissions in men and women increased from 10 to 12; among the women patients the percentage rose from 3.2 to 12.8; that of partial remissions in both men and women, on the other hand, decreased from 51.3 to 37.3 per cent; in men it decreased from 48.7 to 35.3; in women, from 74.2 to 55. This makes a total of about 50 per cent of remissions in both sexes in the partial and complete remissions.

There is no unanimity of opinion regarding the effectiveness of specific after-treatment. The authors' report covers 141 patients treated with the combined

TABLE 9.—*Neurologic Findings Before and After Treatment*

Disturbances	Normal	Improved	Total	Unchanged	Aggravated
Pupils (size and form).....	2	14	16	100	0
Pupils (reaction to light).....	3	9	12	102	2
Facial nerve.....	12	3	15	100	1
Tongue.....	22	6	28	88	0
Speech.....	11	22	33	82	1
Patellar reflex.....	15	8	23	93	0
Achilles reflex.....	14	13	27	89	0
Babinski sign.....	8	3	11	105	0
Oppenheim sign.....	6	3	9	107	0
Muscle tonus.....	2	8	10	106	0
Coordination of extremities.....	26	2	28	88	0
Sensibility.....	16	5	21	95	0
Bladder.....	4	2	6	110	0
Intestines.....	3	0	3	113	0
Equilibrium (Romberg).....	22	6	28	87	1
Writing.....	19	27	46	70	0

method. In the after-treatment arsphenamine was not used, but an arsenical preparation described by Albert and Kalberlah. A short time after the malaria was stopped, or as soon as it was stopped, eleven intravenous injections of the arsenical preparation were given, altogether 3 Gm. The first injection was 0.1 Gm., and from the third to the eleventh injection 0.3 Gm. was given. Table 5 gives the results obtained with both methods of treatment. The combination method was not tried in women.

**Neurologic Findings:** Table 9 gives the neurologic findings in 116 cases before and after treatment.

Table 9 shows that in the largest number of cases the neurologic findings are not greatly altered by the treatment. Improvement in the sensory disturbance of the lower extremities is often observed in the tabetic form of dementia paralytica.

The effect of malarial treatment on intelligence was first studied by Irene Kaufmann, who found that fever exerts a favorable influence on the patient's intellectual ability. The same problem has been studied by other investigators. Pfeifer and von Rohden recorded observations not only on the theoretical intelligence before and after malarial treatment, but also on the practical intelligence, the power of adaptability. Remarkable intellectual improvement was found in all cases except in group 4, in which it sank from an average of 27 per cent before malarial treatment to an average of 16 per cent after treatment. In group 1, among the cured patients, the intelligence percentage rose from 22 to 41; in group 2 a it rose from 14 to 29. This finding is significant when one considers that most of Pfeifer and von Rohden's patients as well as those reported by others came from about the same strata of society.

**Prognostic Criteria:** Under this head the authors discuss the probable therapeutic success with malarial treatment in patients of a certain build and in those with certain clinical symptoms. Their conclusions are that in general the best prospect of cure with malaria is offered by the pyknic type; also that (1) the best prospect for remission is in patients with initial neurasthenic-hypochondriac symptoms; (2) a good remission occurs in patients with a manic-depressive psychosis, especially if of pyknic type; (3) less hope is to be entertained for the expansive, expansive agitated and euphoric-demented types, but greater hope for the pyknic patients in this group; (4) a poor prognosis is to be expected in the dumb, demented patients, especially if they are not of pyknic habitus. An important factor in prognosis is the duration of the disease, as it is in other chronic diseases. The sooner the patient comes under treatment the more favorable is the prognosis. The correlation between duration of the disease and remissions is given in table 15.

In table 15 it may be observed that the best remissions were not obtained in cases in which the disease had lasted a long time; 50 per cent of the patients first appeared for treatment after the symptoms had been present for from one-half to two years. In 95 patients the disease was of less than one-half year's duration; in 54 the duration was over two years.

Hence, the best outlook with malarial treatment is in patients whose symptoms are not of over three months' duration. A relative recovery may be expected

TABLE 15.—*Correlation Between Duration of the Disease and the Remissions*

Duration	Group								No. of Cases
	1	2 a	2 b	2 c	2 d	3	4	5	
Up to 2 months.....	76.7	13.1	5.2	....	....	....	....	1.6	32
Up to 6 months.....	21.0	60.7	34.0	11.1	4.5	2.6	5.8	11.5	63
Up to 1 year.....	3.3	15.8	39.5	41.5	13.6	26.3	29.4	29.5	81
Up to 2 years.....	....	5.2	19.0	22.2	36.4	39.5	35.4	32.8	70
Up to 3 years.....	....	....	....	5.5	13.6	21.1	5.8	13.1	22
Over 3 years.....	....	5.2	1.8	19.4	31.9	10.5	23.6	11.5	32
Total number of cases.....	30	38	58	36	22	38	17	61	300

when the disease has not lasted over one year. When the disease has lasted longer, the best that one may expect is a partial recovery. If the disease has lasted more than two years, malarial treatment is usually of little benefit.

These are not hard and fast rules; there are exceptions. The severity may differ in some patients, although, as Pönitz pointed out, most patients experience an approximately similar course of the disease. However, the tempo of the disease may be mild or severe. In the galloping type, malarial treatment is too late even when employed soon after psychic symptoms have set in. On the other hand, if the disease is of a slower tempo a cure may occasionally be obtained after the disease has existed for some time. Unfortunately, at present there is no way of foretelling the prognostic possibilities in cases of long duration.

The authors discuss also the frequency of dementia paralytica and the duration of institutional care under malarial treatment. They tabulate the number of patients received each year between the years 1926 and 1930, the number who were discharged, the number who died and the number who remained, thus showing the changes under each head before and since treatment with malaria was instituted. They conclude that malarial treatment has not shortened the average stay of these patients in institutions, but rather has lengthened it. It is by far the best mode of treatment available, but has its defects. Side by side with brilliant results, one observes patients with crippled brains, who remain in the hospitals for years; these constitute the larger number.

To avoid this result, the authors argue that early diagnosis and treatment are needed. The treatment should be given, if possible, in the early stages of the disease, when the degenerative changes are at a minimum, and when inflammatory

conditions alone are present. Again, the treatment should be more strictly given to those who can benefit by it; cases that are known to be beyond the influence of malarial treatment should be excluded.

ENCEPHALOGRAPHY AND ITS PROGNOSTIC IMPORTANCE IN THE COURSE OF DEMENTIA PARALYTICA. KARL PÖNITZ, Halle, Germany.

Pönitz believes that encephalography offers a means of foretelling the possible effect of fever treatment in dementia paralytica. It is known that the inflammatory processes may undergo involution; degenerative processes in the early stages may also recover, but destroyed ganglion cells and tracts cannot recover. In the first type of cases a complete remission is possible; in the second type one may expect a remission with defect; in the third type the remaining ganglion cells may take over the functions, but no recovery may be expected. The glial proliferation, which is an attempt to replace the atrophy of the brain, is not evenly distributed, the cerebrospinal fluid fills up the empty spaces, the subarachnoid space and the ventricles enlarge, and thus there develops an internal and external hydrocephalus. In this anatomic condition, created by the cerebral atrophy, encephalography offers an important diagnostic aid in determining, before fever treatment is attempted, the degree of atrophy of the brain and whether or not recovery, or what kind of recovery, may be expected. If encephalography shows unusually dilated ventricles and unusual accumulation of air over the surface of the brain, one can hardly expect a cure without defects. Patients who show advanced deterioration can be excluded from the fever treatment; hence, the importance of encephalography in these cases.

Encephalography is not without danger; ordinarily there are considerable after-effects, and death has sometimes taken place. However, encephalography has little effect on patients with this disease, and many investigators agree that in these cases the procedure is harmless.

Pönitz also suggests that most of the after-effects of encephalography are due to injecting too much air. He uses the lumbar in preference to the occipital route, and often injects very little air; he finds it unnecessary to empty all the fluid. In only a few cases is it necessary to inject more than 100 cc. of air, from 40 to 50 cc. often being sufficient to give good results. Occasionally, before the injection the patient is given avertin; in a large number of cases Pönitz has given a small dose of morphine and scopolamine hydrobromide one-half hour before. By observing these rules one eliminates after-cramps, vascular disturbances and vomiting. In about 50 per cent of the cases the patients complain of pain in the back and, when more than from 60 to 80 cc. of air is injected, of headaches. All discomforts disappear in a day.

The expectation that on account of the atrophy of the brain a large quantity of air would accumulate in the subarachnoid space was substantiated. Pönitz believes that this is due to the small volume of air injected and also to the many adhesions of the meninges which do not permit the air to pass.

Pönitz failed to obtain results with this method in about 10 per cent of his cases. In some the ventricles failed to fill. This does not argue against a diagnosis of dementia paralytica. In some cases a second injection filled the ventricles. Some investigators maintain that it is not unusual to find a failure in filling the ventricles in dementia paralytica when the air is injected by the lumbar route; adhesions may be responsible for this. In some cases only one ventricle will fill. Often an asymmetry of the ventricles is found; the left is usually somewhat the larger. Wartenberg raised the question whether in dementia paralytica the left side of the brain in the average case is not more involved than the right. Pönitz has never found normal lateral ventricles in clinically established cases. A very slight dilatation may be found in cases that show barely any psychic anomalies. This can best be observed in the fronto-occipital position. The dilatation manifests itself first by a rounding of the upper and lower ends, and the winged butterfly shape becomes more oval. Mild changes, when found, cannot be utilized for prognostic purposes; however, they are useful for diagnosis.

The exact size of the ventricles cannot be determined. It can be spoken of only in relative terms; e. g., "there is an indication of dilatation, a definite dilatation or a marked dilatation." When the hydrocephalus is large, one must assume the presence of considerable atrophy of the brain, replacement of which is impossible. On the other hand, a small ventricle does not necessarily indicate that recovery will take place without leaving some defect. Relatively small circumscribed lesions of the brain may cause considerable psychic disturbance; again, the tempo of the morbid process must be considered; if it is rapid, even though hydrocephalus is mild, treatment may be of little service. However, ordinarily it can be said that when a mild ventricular dilatation is present there is a possibility the fever treatment will bring about a cure without leaving behind any psychic defects, and that there will not be any considerable, permanent lowering of the intellect; but that when the ventricles are considerably dilated, a cure cannot be expected without defects, except perhaps when in addition to the dementia paralytica the history discloses epileptic attacks during earlier years or there has been a cerebral trauma.

STUDY OF THE CEREBROSPINAL FLUID. OTTO REHM, Bremen, Germany.

1. Cell Forms: Rehm is concerned mainly with the types of cells in the cerebrospinal fluid and their distribution in different diseases. Although the material is not large, the observations are significant. The fluid was examined in a Fuchs-Rosenthal counting chamber. The chamber must be filled with the fluid at the bedside; otherwise the count may be inaccurate, because some cells may sink to the bottom. Staining with saponin is not advisable, as it causes crumbling and turbidity of the fluid. Ordinarily, examination of one chamber is sufficient. When the fluid is not kept too long in the chamber, the red cells can be easily distinguished from the lymphocytes without the addition of saponin. Large lobulated cells cannot be distinguished from large lymphocytes. On the other hand, phagocytes are easily recognized. Gitter cells usually are not recognized. The lymphocytic nucleus has a tendency to be extruded from the cell body while in the chamber, and thus the body appears as an appendage of the nucleus. Rehm limits discussion in this article to the types of cells in the fluid, and does not discuss the relative numbers.

The investigation was made by Alzheimer's method: Two cubic centimeters of fluid is received in 96 per cent alcohol. A floccular turbidity is formed, and the fluid is centrifugated; the sediment is carefully removed into another glass containing pure alcohol; after two hours the alcohol is replaced by alcohol and ether, and two hours later by ether; the sediment is then embedded in pyroxylin (celloidin), sectioned as thin as possible and stained. The best stain is methyl green-pyronine (Unna-Pappenheim). Toluidine blue and hematoxylin can also be used.

Normally, there are found in the spinal fluid: (1) Small lymphocytes, the size of a red cell or smaller. The nucleus fills nearly the entire cell body and stains deeply. The small lymphocytes, in size and appearance, are exactly like the blood lymphocytes. (2) Large lymphocytes larger than red cells; otherwise they resemble the small lymphocytes. At times there is a zone of transparency around the nucleus. (3) Large polymorphonuclear cells, which resemble monocytes in the blood and are probably homonymous with them. They are considerably larger than the large lymphocytes. The nucleus is swollen and often sausage-shaped; unlike that of the lymphocyte, the nucleus in this cell does not nearly fill the cell body; it stains more faintly than that of the lymphocyte. The nucleolus is distinct. At the border of the cell membrane there is at times an indication of granulation. (4) Histogenous cells, which are usually very large. In some the nucleus fills the entire cell body; in some the cell body ends with an offshoot, which comes gradually to a point. There is often a transparent zone around the nucleus. The protoplasm stains uniformly. The nucleus is pale. The nucleolus is distinct. (5) Gitter cells, which are very few. They are much larger than any other cells in the normal spinal fluid. The contours of the cells are exceptionally delicate, so that at times the staining can barely be observed. There are no granules in the plasma.

The body is irregular in form and has many pouches. Aside from the nucleus, these spaces often make up the entire cell. A delicate wall surrounds this honeycomb. The spaces have different shapes and are filled with a mass; some of these stain lightly, and others stain well. The nucleus looks like that of the histogenous cell. In most of the cells it is round, but in many it is pushed near the wall and is irregular in shape. Some important forces must have been in action to displace the nucleus. It may be that the cell has the power to receive within itself substances which possess colloidal properties other than those of the plasma mass of the cell. The received substances are absorbed in the smallest quantities. They are probably quickly destroyed in the cerebrospinal fluid.

As to the source of the different cells, the lymphocytes, both large and small, are similar to the lymphocytes in the blood. The large lobulated cells are similar to the monocytes of the blood. Histogenous and gitter cells ordinarily are not present in the blood; these cells most certainly come from the tissues; they resemble the connective tissue cells of the pia. Gitter cells are occasionally present in the pia. Spielmeyer and most investigators describe gitter cells as histogenous, and consider them to be, like macrophages, wandering cells. If this assumption is correct, the gitter cells of the spinal fluid can come from the pial tissues just as do the hematogenous cells. Whether under normal conditions the spinal fluid is capable of such attraction is a question. Apparently it is more likely that the gitter cells are formed in the spinal fluid from connective tissue cells, like the monocytes in the fluid, since even under normal conditions they take up to a certain extent the altered albuminous substance, and after changing it chemically give it up shortly before they themselves are destroyed. Considering the shape of the cell, they cannot come from the choroid plexus or from the ependyma, since such cells are not found there.

The histogenous cells are products of the pia and can be found in all tissues. After a destructive process and after death the number of these cells in the spinal fluid is considerably increased.

The source of the lymphocytes and monocytes has so far not been established. The nearest guess is that they are derived from the blood. Morphologically, they are the same cells as those in the blood. Different types of lymphocytes are always found in the arachnoid and in the pia, so that it is possible to think of them as wandering out from the blood vessels and lymph through the tissues into the spinal fluid. In denying this conception one must assume that they come from the connective tissue. Against such an assumption speaks the form of the cell as well as the staining of the nucleus. Therefore it is most likely that they are derived from the blood. It can be assumed that the spinal fluid is chemotactic to these cells. A special selection also takes place, for the number of cells in the fluid is not the same as the number in the blood. These cells are also found in the pia. From these considerations the conclusion is reached that the lymphocytes probably represent blood cells which from biologic and chemotactic causes have wandered into the cerebrospinal fluid; the large lobulated elements are the result of a special selection in the wandering out of the cells. The other cells, fewer in number, are histogenous, a product of growth of the tissue or cast-off cells, which partly assume a special physiologic function in the changing of an albumin-like substance in the cerebrospinal fluid into some other colloidal and chemical substance.

Death of the cells in the spinal fluid must proceed slowly. Death of the histogenous cells can often be observed under the microscope. The cell body disappears, the nucleus loses its staining, the chromatin becomes homogeneous, and the nuclear membrane melts away and breaks up. Degeneration of the lymphocytes is observed in inflammatory conditions of the pia; the nuclei become laky and homogeneous and break up into pigments.

In the normal cerebrospinal fluid these degenerative changes are not observed, although it is probable that here, too, the lymphocytes undergo similar degeneration. That the destruction of the lymphocyte is not observed is due to the fact that normally these cells enjoy a long life, and the renewal of the lymphocytes is slow. Occasionally, mitotic nuclear division can be observed. This, too, speaks for the conclusion that the lymphocytes are capable of living in the spinal fluid.

It may therefore be concluded that: the histogenous cells undergo comparatively quick destruction; the lymphocytes and monocytes have a long existence, and in the normal fluid their destruction takes place by means of a breaking up of the nuclear substance into chromatin granules. The pigment observed in a stained specimen represents the end-product. The rods represent the broken-up nuclear membrane exclusively or mainly of the histogenous cells.

Very often the cells in the fluid, both lymphocytes and histogenous cells, show a tail-like change in the plasma body. Cells with this change also are found in normal fluid. The nuclei resemble the large, small and lobulated nuclei. There is no reason to consider these cells as of special type. The assumption is justified that the tail-like feature represents changes that have taken place, or that the cells react differently to the spinal fluid; in other words, the change in the cell body

*Varieties of Cells in the Cerebrospinal Fluid in Different Diseases*

Disease	Erythrocytes	Leukocytes	Small Lymphocytes	Large Lymphocytes	Large Lobulated Cells	Tail-like Lymphocytes	Histogenous Cells	Honeycomb Cells	Mast Cells	Gitter Cells	Phagocytes	Plasma Cells	Granular Cells	Rods
Herpes zoster.....	..	..	+	+	+	+	+	..	..	+	..	..	..	..
Alcoholic polyneuritis.....	..	..	+	+	+	+	+	..	..	..	..	..	..	..
Pellagra.....	..	..	+	+	+	+	+	..	..	..	..	..	..	..
Psychopathy.....	..	..	+	+	+	+	+	..	..	..	..	..	..	..
Schizophrenia.....	..	..	+	+	+	+	+	..	..	..	..	..	..	..
Manic-depressive psychosis.....	..	..	+	+	+	+	+	..	..	..	..	..	..	..
Acute delirium.....	..	..	+	+	+	+	+	..	..	..	..	..	..	..
Meningitis serosa.....	..	..	+	+	+	+	+	..	..	..	..	..	..	..
Meningitis tuberculosa.....	+	+	+	+	+	+	+	..	..	..	..	..	..	..
Meningitis purulenta.....	..	+	+	+	+	+	+	..	..	..	..	..	..	..
Imbecility and idiocy.....	..	..	+	+	+	+	+	..	..	..	..	..	..	..
Cerebral infantile paralysis.....	..	..	+	+	+	+	+	..	..	..	..	..	..	..
Encephalitis infantilis.....	..	..	+	+	+	+	+	..	..	..	..	..	..	..
Encephalitis epidemica.....	..	..	+	+	+	+	+	..	..	..	..	..	..	..
Encephalitis of Wernicke.....	..	..	+	+	+	+	+	..	..	..	..	..	..	..
Commotio cerebri.....	..	..	+	+	+	+	+	..	..	..	..	..	..	..
Cerebral apoplexy.....	+	+	+	+	+	+	+	..	..	..	..	..	..	..
Encephalomalacia.....	..	+	+	+	+	+	+	..	..	..	..	..	..	..
Senile dementia.....	+	+	+	+	+	+	+	..	..	..	..	..	..	..
Alzheimer's disease.....	..	..	+	+	+	+	+	..	..	..	..	..	..	..
Huntington's chorea.....	..	..	+	+	+	+	+	..	..	..	..	..	..	..
Tumor cerebrospinalis.....	..	..	+	+	+	+	+	..	..	..	..	..	..	..
Multiple sclerosis.....	..	..	+	+	+	+	+	..	..	..	..	..	..	..
Cerebral emboli.....	..	..	+	+	+	+	+	..	..	..	..	..	..	..
Late syphilis.....	..	..	+	+	+	+	+	..	..	..	..	..	..	..
Cerebrospinal syphilis.....	..	..	+	+	+	+	+	..	..	..	..	..	..	..
Tubes.....	..	..	+	+	+	+	+	..	..	..	..	..	..	..
Tabetic dementia paralytica.....	..	+	+	+	+	+	+	..	..	..	..	..	..	..
Dementia paralytica.....	..	+	+	+	+	+	+	..	..	..	..	..	..	..
Postmortem changes.....	..	..	+	+	+	+	+	..	..	..	..	..	..	..

is an effect of time. Post mortem, the spinal fluid does not show an increase in the tail-like cells. These cells do not take the stain well.

Red cells do not belong normally in the spinal fluid. They are often found as a result of the puncture. Red cells in the fluid before puncture show changes which are to be considered as a manifestation of disintegration. The cell shrinks, the stain becomes pale, and finally the cell breaks up into small particles that still retain a shiny red color. This type of cell disintegration is especially marked in strongly inflammatory and destructive processes, such as in cranial hemorrhage. The same type of disintegration is also observed in phagocytes. Another, perhaps a slower, method of destruction of red cells in the spinal fluid is that the cell becomes larger and therefore takes the stain less; it then loses its form, forms a kind of ring and resembles a gitter cell. Finally, it becomes pale, and dirty red-stained shadows are the remains of the disintegration.

The types of cells in the spinal fluid in diseases of the central nervous system are given in the table. They resemble closely those in normal spinal fluid. Exceptions are a case of pellagra and one of polioencephalitis haemorrhagica of Wernicke. In the latter, only small lymphocytes were found. In the different diseases and in the functional psychoses there were honeycomb cells. These honeycomb monocytes, according to their character, are blood cells which, like gitter cells, take up colloidal substances in the spinal fluid. It is probable that further investigations will justify considering them as normal cells in the spinal fluid. They differ from gitter cells in their smaller size and mainly in their large and lobulated nucleus. They usually contain only a few honeycombs.

In some meningeal diseases macrophages occur. They have the same appearance and structure and stain like the gitter cells. Probably they are derivatives of connective tissue, and their function is to remove necrotic cells from the spinal fluid. They do not devour cells that have begun to degenerate, but apparently attack exclusively healthy cells. Erythrocytes, leukocytes, lymphocytes, monocytes and plasma cells are phagocytosed. In the process of digestion the body of the ingested cell disappears first. The nucleus may be preserved for some time. It then becomes homogeneous, and finally only a stained shadow can be observed in the honeycomb. Chemotactic stimuli change histogenous cells into phagocytes, just as they do gitter cells. Why the histogenous cells do not normally but only in cases of meningeal disturbance change into phagocytes is not clear. The stimulus must lie in the fluid. Soon after death the phagocytes which devour desquamated cells appear in large numbers.

In a number of diseases plasma cells are found in the spinal fluid. They are derived from the blood. They are somewhat larger than lymphocytes; at times they are tail-shaped, and the plasma stains more deeply than in the lymphocytes.

In some cases there are granular cells. They are essentially monocytes in which are present a large number of granules of light color, and they resemble the end-product of broken-up red cells. They are also found in cases in which no red cells are present. It is not to be assumed that the granules are picked up from the spinal fluid, but rather that they are the result of a strongly stained plasma substance. They are few in number.

Plasma cells were found in the spinal fluid in a case of serous meningitis, which was probably of allergic origin. Otherwise they are found only with syphilitic and suppurative meningitis.

In cerebral hemorrhage the spinal fluid contains leukocytes which have picked up many granules. The leukocytes have become phagocytes. They come from the blood, and their function is to disinfect the spinal fluid.

Suppurative and tuberculous meningitis, together with syphilitic meningitis, show the presence of many types of cells in the spinal fluid. The leukocytes play an important part. In tuberculous meningitis there are always red blood cells also. In senile dementia, erythrocytes and leukocytes are never absent. Here, too, granular cells of the monocyte type are present. When there is no hemorrhage, the presence of erythrocytes can be explained only by diapedesis.

In tumor of the brain or cord the spinal fluid often contains mast cells. They are filled with pigment granules, which often cover the nucleus; they are of oval shape. Structural characteristics that are derived from the tumor can occasionally be observed, but not always. It is not unlikely that a few cells may be assigned as tumor cells. In tumors of the choroid plexus Foerster has often found tumor cells in the cerebrospinal fluid by ventricular puncture.

It is uncertain where the mast cells come from. Nissl was of the opinion that they are hematogenous, but they probably are also derived from the adventitia. It is said that in dementia paralytica they are also found in the circulating blood. In the pia there are connective tissue cells that resemble mast cells. In the choroid plexus the mast cells appear to be hematogenous. Foerster has found plasma cells in the spinal fluid in tumors of the brain.

Dementia paralytica with meningitis shows the largest variety of cells in the spinal fluid. All kinds of cells may be found except mast cells. It is important that in dementia paralytica mast cells are abundant in the pia. Apparently they

occur in the spinal fluid only when the growing tumor presses the inflamed adjacent tissue directly into the subarachnoid space and brings about a separation of the tissue. In uncomplicated cases of tabes plasma and granular cells are found, but no gutter cells. In tabes leukocytes are present only during a crisis; otherwise they are not present.

In a patient with manic excitement examined half an hour after death, there was a condition similar to meningitis or dementia paralytica. The leukocytes and granular cells were the only types missing. At death, therefore, simultaneous meningeal changes take place which are connected apparently with a loosening of the tissue, which acts biologically like an inflammation of the pia and at the same time gives up a considerable number of histogenous cells.

REACTION OF THE NERVE PARENCHYMA TO ENDOGENOUS AND EXOGENOUS NOXAE. KARL SCHAFFER, Budapest, Hungary.

Schaffer calls attention to the systemic neuron structure and the ectomesodermal separation line produced by the glial membrana limitans. Without the conception of a neuron there can be no profitable pathologic study of the central nervous system. The difference between the ectodermal and the mesodermal elements in the central nervous system enables one to understand diseases in this field.

1. Endogenous changes in the central nervous system occur in hereditary systemic nervous diseases. The disease bears an ectodermal character, affecting either the neuronal, the neuroglial or both elements in a progressive primary degeneration. The ectodermal character in these cases is indicated by the disturbed and faulty development, hypogenesis and dysgenesis of the central nervous system. There occur falsely oriented ganglion cells and abnormally formed, monstrous glia cells; finally there are heterotopic changes; these are the so-called microstigmas of abnormal development. There are also macrostigmas: hypoplasia of certain central segments. These stigmas of abnormal development indicate an abnormal predisposition of the central organs, a condition which Schaffer designated as abiogenesis, which, with its subnormal foundation, brings about a progressive elective degeneration of the ectodermal elements, a condition which, since Gowers, has been described as abiotrophy. Abiogenesis indicates subnormally developed central organs endowed with a power of life that is too brief, in which the neural elements incapable of living are destroyed.

Abiotrophy can be observed clearly when the long neuron systems are diseased. The process takes origin in definite neuronal centers and limits itself to definite systems. It is a condition in which certain isolated bilateral symmetrical systems die. Schaffer calls this abiotrophia neuronalis. Since this condition has its origin in a corresponding segmental center, it becomes evident that this elective process is based on three factors: (1) the electivity of the germinal layer, for the ectodermal neurons alone degenerate while the mesodermal elements are entirely spared; (2) the systemic electivity, for the nervous system always dies proportionately to the given hereditary systemic disease; (3) the segmental electivity, for commensurable with the degenerated systems the starting point of the degeneration is always in a segmental center. Therefore a hereditary systemic disease appears anatomically characterized as ectodermal, segmentally centrally bound and systemically presenting progressive degeneration of the central nervous system. The clinical picture of such a disease depends on the systems involved. If the pyramidal tracts are involved, the symptoms will be those of spastic heredo-degeneration; if the spinobulbomesencephalic motor nuclear system is diseased, there develops spinobulbomesencephalic amyotrophy; in diseases of the voluntary tracts there will be amyotrophic lateral sclerosis; degeneration of the spinocerebellar tracts produces the picture of Friedreich's disease; in diseases of the cerebellar neurons Marie's heredo-ataxia appears; diseases of the extrapyramidal systems give the picture of hereditary late chorea or dystonia lordotica.

There may also be a primary elective disease of the second neuro-ectodermal elements, the neuroglia, as an abiotrophia neurogliosa, in which the picture described by Krabbe-Scholtz, familial sclerosis of the brain, develops. Here the neuronal

elements may be affected only secondarily. In these cases are found spastic paralysis and progressive dementia. Since the glia cells do not form a system like the long neurons, primary system degenerations are lacking; they can develop only secondarily, as when the glial proliferation presses on the pyramidal tracts in the hemispheres. Yet here the glial proliferation, aside from being on both sides, has its starting point in the periventricular spaces. It is known that the periventricular ependyma is a most important region in the development of the brain, for here, in the susceptible matrix ventricularis, lie concealed Schaper's indifferent elements; this region offers not alone a normal development, but on the basis of the presence of dysgenic embryonic glia also a pathologic development. Finally, the third possibility is that the primary ectodermal degeneration may affect at the same time both the neuronal and the neuroglial elements, in which case the picture of familial idiocy will be present.

These considerations indicate as a positive that the familial endogenous nervous diseases are elective diseases of the ectodermal elements, and as a negative that the mesodermal elements are not involved in the sense of a primary active disease, for the vascular infiltration shows only breaking up of glia cells; if plasma cells are also present this is only a reactive manifestation as a result of a large and rapid destruction. This cannot be considered an inflammation.

Summing up, it can be said that generally endogenous diseases of the central nervous system are recognized: (1) by a defectively developed base, abiogenetic neuro-ectoderm; (2) by elective degeneration of the ectodermal elements, abiotrophy, especially when the neuron systems are involved; (3) by the primary uninvolved of the mesodermal elements. Schaffer designates this group of diseases as ectodermogeny. Fundamentally one deals with a disease of the germinal layer.

2. Entirely different changes are observed when exogenous noxae are present. Here infectious and toxic influences are at play; hence a different kind of histopathologic pictures may be observed.

Infectious noxae, on the one hand, are granulomatous inflammations; on the other hand, simple inflammations. Pette divided the latter into two groups: (1) Meningeal infectious diseases brought on by suppurative inflammatory diseases in other parts of the body. They are toxic diseases (tetanus, diphtheria and botulism). The disease first attacks some other organ. The nervous system is affected secondarily. (2) "Acute infections of the nervous system"; histologically they show inflammation that primarily and exclusively affects the nervous system. There are two types, one that affects mainly the gray substance and one that affects mainly the white substance. In the first type of cases Pette included experimental herpes encephalitis, epidemic encephalitis, acute anterior poliomyelitis, rabies, Borna disease, zoster and certain forms of Landry's paralysis. In the second type are included disseminated encephalomyelitis, acute multiple sclerosis, certain forms of diffuse sclerosis and J. Baló's encephalitis periaxialis concentrica. Transition from one type to another does not take place.

Seifried and Spatz maintained that Borna disease, epidemic encephalitis, acute anterior poliomyelitis and rabies might present an anatomic similarity in that the inflammatory changes of the central nervous system could extend to the outer and inner surface while leaving the central parts free. If this is the case, the assumption is justified that the virus is carried by the cerebrospinal fluid. But the fact that the meninges are intact refutes this assumption.

Experimental herpes encephalitis is a striking example of a true neural infection. After experimental production of a keratoconjunctivitis, the ciliary ganglion becomes inflamed; then the gasserian ganglion is affected; then the pons on the affected side; then the trigeminus; then the cerebellum, and finally the brain. If the herpes virus is injected into a peripheral nerve, myelitis develops, with the primary lesion corresponding to the inoculated nerve. From this point the process may spread to the entire central nervous system. Schaffer had shown these findings to be true of human rabies forty years ago.

The diseases mentioned not only are similar in neurotropism, but are also somewhat related histologically in that the inflammatory process affects the gray

substance, although the white substance is not entirely spared. There are two possibilities: In massive intoxication necrosis regularly appears in the gray and white substances, while in cases with a milder virulence the course is that of a simple inflammation. This has been found to be true for rabies and for the different types of herpes. In the latter, according to Pette, there is, in addition to a meningeal and vascular proliferation as a mesodermal reaction, also proliferation of the glia, nominally the Hortega elements. From the glial reaction and from the disease of the parenchyma Pette concluded that these changes may be the direct result of the virus. According to Schaffer, the two types of changes are present; the ectodermal and mesodermal are coordinated, for they are the result of the same cause and appear at the same time. The meningeal inflammatory reaction is moderate, and is conditioned by the localization of the process in the parenchyma. In acute anterior poliomyelitis and in herpes at the beginning there are present a number of leukocytes. The nerve cells are more affected in poliomyelitis than in herpes and show neuronophagia. Here, too, belongs epidemic encephalitis. Although the herpes and the zoster virus are not identical, the process seems to be the same; the spinal ganglia show acute lymphocytic and plasmocytic infiltration, and the inflammation extends to the cord. The primary point of attack of the zoster virus is either the skin or the nervous system; the latter is supported by the fact that the vesicles are in the nerve distribution.

Acute infections of the central nervous system involving mainly the gray matter show mesodermal and ectodermal reactions, which may have different development in the different forms. Epidemic encephalitis may serve as an example. Stefan Környey found that the degeneration and disappearance of the substantia nigra cannot be explained by the localization of the inflammatory process. The substantia nigra often disappears without inflammation being evident; in such cases it may well be assumed that the inflammation has run its course. But it must be noted that the tracts that pass through the substantia nigra (tractus pallidosubthalamicopedunculares) remain unaffected; this indicates that in the area of the substantia nigra there is no inflammatory lesion; otherwise there would be a secondary degeneration of the tracts. Környey concluded that the virus of epidemic encephalitis has a strong affinity for the substantia nigra. Schaffer designates this as ectodermotropy.

Of the acute inflammatory diseases affecting mainly the white substance, Pette mentioned scarlet fever, vaccinia, variola, typhoid, angina and gastro-enteritis. Although symptomatically the picture may vary, the pyramidal tracts are often involved; in severe and diffused types in children, involvement of the extra-pyramidal system may occur. Histologically, there may be complete or incomplete demyelination. A mesodermal inflammatory reaction seldom fails to occur.

Among the noxae responsible for exogenous disease, alcohol takes the lead. It affects the connective tissue and the vascular system, and brings on meningeal thickening and at times endothelial and perithelial proliferation. It also possesses affinity for certain parts of the central nervous system; the parasympathetic or peripheral nerves may be involved. Thus, it seems that the noxa has a chemical affinity for certain ectodermal parts. It is to be noted that the disease takes place in association with meningeal and vascular changes which spring from the same source.

As to the question whether a differentiation can be made in the tissue structure between exogenous and endogenous diseases of the central nervous system, it must be said that this can be accomplished only by structural analysis of the changes in the process of the disease; the results may not always be definite, for endogenous and exogenous diseases may occur simultaneously. The structural analysis depends on which of the germinal layer elements are changed by the disease, and this will determine the type of the disease. In the central nervous system, therefore, one speaks of ectodermal and endodermal changes, from a typologic point of view. The next question is that of the special changes observable, that is, the sum total of the finest structural changes. When the two categories of changes are established, it is possible to recognize the nature of the disease process.

Utilizing the analytic principles, it may be said that those of the typologic group, the specific ectodermal changes, are the purest, for primarily neuronal or neuroglial elements are exclusively diseased. Yet a similar and simultaneous disease associated with the ectodermal elements is also possible. Because diseases of the ectodermal neuronal elements occur in a segmental systemic form, and since according to a given hereditary disease process there develops an elective degeneration of a given neuron system belonging to a given segment, it presents a structural form of the ectodermal type which Schaffer calls ectodermogenous changes (abiotrophy). The neuronal abiotrophy can be recognized by the following triple electivity: (1) the germinal layer; (2) the system; (3) the segment.

Exogenous diseases of the central nervous system present another picture. Here the primary active change takes place in the mesodermal elements. It may occur in two forms: 1. The blood vessels may be diseased, mainly from the effects of poison (alcohol, nicotine, lead, etc.), presenting a picture of atherosclerosis with fibrous and hyaline changes in the vascular wall and bringing about mainly irregular areas of softening and hemorrhage. Here total necrosis develops, involving both ectodermal and mesodermal elements. 2. There are two kinds of the second form, simple inflammation and granulomatous inflammation. Both forms are brought on by a virus causing an inflammation that affects the blood vessels. The primary active changes are connected with the skin and the blood vessels. These changes are either localized or diffuse; they respect neither segments nor systems and thus form a picture absolutely opposite to that of the elective ectodermogenous changes.

Certain exogenous influences may bring about structural changes which typologically may be mesodermal and ectodermal, i. e., a mixture. Thus Pette's acute infection of the central nervous system as a neurotropic inflammatory form is capable of bringing about typical inflammatory changes in addition to direct glial reactions. In the effects of poisons (alcohol) and of toxins (diphtheria and epidemic encephalitis) it can be observed that certain nerve centers are preferably affected.

The last-mentioned group represents typologic diseases of the central nervous system with mesodermal and ectodermal changes, in which structurally, in addition to the inflammatory changes, the endoperithelial proliferation (alcohol) and the granuloma formation, a pure central parenchymatous and system degeneration is also produced.

#### OLIGOSYMPTOMATIC MESAORTITIS AND SYPHILIS OF THE CENTRAL NERVOUS SYSTEM. HERMANN SCHLESINGER, Vienna, Austria.

In the group of late syphilitic diseases belong tabes, dementia paralytica, mesaortitis, arthrosyphilis tarda (H. Schlesinger), apparently some diseases of the glands of internal secretion and perhaps also disease of the lungs (Rossele). Late syphilis often attacks only one organ system, sparing the rest of the body. However, the simultaneous involvement of the central nervous system and the aorta is of frequent occurrence, while arthrosyphilis tarda occurs without the aorta or the central nervous system being involved. It has been found anatomically that in at least one third of cases of syphilis of the central nervous system there is a mesaortitis.

The symptoms in a fully developed case of syphilitic mesaortitis are well known, and the diagnosis can be established with considerable certainty. Lately there has been described a median necrosis of the aorta that is not of syphilitic origin, but which resembles closely syphilitic mesaortitis (Erdheim); the clinical picture of this disease is not known. Apparently it should not differ much from syphilitic aortitis.

The manifestations of a classic mesaortitis are: a systolic murmur over the ascending aorta, accentuation of the second aortic sound and normal or subnormal blood pressure. Roentgenologically, there is a dilatation of the ascending aorta. Symptoms of irritation—aortalgia—are also present. A positive Wassermann reaction occurs in only two thirds of the cases. In a very small group of cases the blood pressure remains permanently increased.

Anatomically, the changes are usually limited to definite parts and are sharply outlined. The favored spot is the ascending aorta, which is often circularly dilated. Aneurysmal bulgings of the aorta, in the largest number of cases, are of syphilitic origin.

Schlesinger has found that only in a fraction of cases of mesaortitis are the classic symptoms present in their entirety; post mortem, a large number of aortic diseases are observed that were unrecognized during life. This is especially true of neurosyphilis. A considerable number of specific aortic diseases run a symptomless course. Often roentgen examination is the first to disclose the dilated aorta. A difference of 1 cm. in the width of the ascending and the descending aorta is accepted as indicative of mesaortitis. In other cases the systolic murmur over the aorta, together with the accentuation of the second aortic sound while the blood pressure remains normal, and the presence of central syphilis permit the recognition of syphilitic aortic changes. The evidence of an aortic insufficiency without a history of preceding endocarditis, in a patient under 50, and the presence of cardiac dyspnea in a patient under 50 without toxic or infectious damage to the heart muscle have the same significance. An aneurysm of the aorta without traumatic etiology is sufficient, in the presence of syphilis of the central nervous system, to indicate the existence of a syphilitic aortic disease.

In the symptoms of mesaortitis with central syphilis, aortalgia and stenocardia are especially noted. The aortic pain has a special localization and is of a peculiar quality. It is usually felt retrosternally, mainly behind the lower sternal end. It is burning, boring, cutting or pressing, at times lasts for hours, occasionally radiates to the shoulders and the upper arms and is brought on under the same conditions as stenocardial attacks, but it also often comes on without any immediate provocation. This pain differs from stenocardia in the duration of the attack and the absence of the feeling of impending death. The pressure point over the cervical plexus described by R. Schmidt and others is inconstant. It is often absent. The cause of this peculiar type of pain is not clear. It occurs in toxic injury to the blood vessels, especially in nicotine intoxication; otherwise, almost exclusively in syphilitic mesaortitis. Schlesinger thinks that the pain in syphilitic aortitis is caused by involvement of the periarterial plexus. In mesaortitis there is regularly a considerable thickening of the adventitia, and larger or smaller bands of connective tissue over the vessels of the pericardium. Since the nerve plexus surrounding the aorta is thick, partly winding directly around the blood vessel, it could receive considerable injury through the pathologic process.

An entirely different interpretation is to be given to the stenocardial attacks in mesaortitis. Post mortem, in cases of angina pectoris, there is always a wall-like swelling around the coronary orifices or a shrinking and considerable narrowing of the branching point, so that no other explanation for the stenocardial attacks is possible than that the coronary blood vessels have undergone a change at the branching point. Complete closure of a coronary artery and considerable changes in others are repeatedly observed in cases of angina pectoris.

Although patients with syphilitic aortitis often suffer from aortalgia and stenocardial attacks, it is seldom that such complaints are encountered in patients with syphilis of the central nervous system. It is rare for a patient with central syphilis to die from an attack of angina pectoris, although coronary changes are present also in these cases. On the other hand, there is often weakness of the muscles of the heart, with a cardiac dyspnea that may reach the severest form. Decompensation, with all its manifestations, is a typical terminal process in neurosyphilis.

Why the two types of pain present in aortitis are lacking in central syphilis, while the other symptoms are present as in mesaortitis without central involvement, is not entirely clear. Schlesinger thinks that it may be analogous to the loss of sensibility for pain often observed in neurosyphilis, as in tabes, in which there is a diminished sensation of pain when the ulnar nerve, the bulbi, the testes or the periosteum is pressed. To a similar degree the fibers coming from the aorta or the fibers from the heart going to the central nervous system may be functionally

affected. The conduction anesthesia stops the transmission of painful sensations from the vascular system to the central nervous system. The damage to the sensory part of the reflex arc prevents, perhaps in many cases, development of attacks of angina.

Schlesinger calls attention to the interesting fact that oligosymptomatic central syphilis is often found together with fully advanced mesaortitis; on the other hand, advanced symptomatic central syphilis often accompanies oligosymptomatic mesaortitis. Therefore, when both involvements are present the syphilis usually shows a greater preference for one of the two regions involved. An explanation might be that in this part of the body there took place originally a stronger spirochetal invasion to which the patient was incapable of offering a corresponding resistance, while the gradual development of protective bodies immunized the rest of the body. Thus, in simultaneous diseases of the aorta and the central nervous system one organ could be more involved than the other. The less damaged organ, by means of the local immunization process, could hold back—although not sufficiently—the more severe lesion of the spirochetes. The relatively mild disease shows itself clinically as an oligosymptomatic type, and shows very little tendency to progression. The clinical formula, therefore, is that severe syphilitic diseases of the central nervous system usually protect the aorta from extensive lesions by *Spirochaeta pallida*, and vice versa. The milder disease, which is more stationary, represents the oligosymptomatic type.

The prognosis in cases of mesaortitis with central syphilis is generally more favorable than in those without this complication. The diseased blood vessels often produce no symptoms. Wagner-Jauregg reported on the relative benignity of aortitis in dementia paralytica. Only when the coronary arteries are also considerably involved or an interstitial myocarditis is present may death take place in the early stages.

The practical question is whether fever therapy is dangerous in diseases of the blood vessels. A general answer is not possible. Consideration should be given to the different localizations of the aortic process and to its anatomic forms. An aneurysmal dilatation is a contraindication to this treatment. So also are diseases of the coronary arteries. Also in weakness of the heart without coronary involvement or in advanced age the treatment is contraindicated. On the other hand, the presence of a compensated aortic insufficiency without coronary symptoms is no contraindication to malarial treatment.

In conclusion, it is to be noted that central syphilis and syphilitic aortitis are often found in the same patient; yet one disease alone usually produces the typical symptoms; the other disease appears only as an oligosymptomatic type and remains more stationary. This can be recognized clinically. More severe disease of an organ system and local immunization processes can explain this. Aortalgia and stenocardia are often absent in mesaortitis with central syphilis, most probably as a result of degenerative processes in the periarterial nerve plexus. The severity of the arterial involvement is an indicative factor in the decision for or against fever therapy.

#### SYMPTOMATOLOGY OF ORGANIC DISEASES OF THE INTERBRAIN: A USEFUL DIAGNOSTIC INTERBRAIN SYNDROME. G. STERTZ, Kiel, Germany.

In 1929, Stertz called attention to the following syndrome in diseases of the interbrain: (1) somnolence; (2) a peculiar psychic disturbance; (3) pupillary symptoms in the sense of alternating differences, and a temporary or permanent diminished reaction to complete failure of reaction to light; (4) bladder disturbance; (5) vegetative disturbances, such as fluctuation in weight, menstruation anomalies, etc., although these are less often observed. Partial optic atrophy, disturbances of the ocular muscles, extrapyramidal and pyramidal symptoms and cerebellar manifestations appear when the process extends more orally or caudally. General increased intracranial pressure, with or without stupor, was absent in the further course of the case. The diagnosis was substantiated in a number of cases by observations at autopsy.

The psychic disturbance in this syndrome is essentially a sinking of all psychic energies, which is expressed in all psychic activity. In the field of thought there is a kind of dementia; in the field of memory there is a condition similar to that of Korsakoff's disease; euphoria, apathy and lack of initiative are observed which may develop into stupor.

Stertz reports 24 cases of disease of the interbrain in which this syndrome was prominent; among these were 7 cases of tumor of the brain, 1 of abscess of the brain, 2 of hydrocephalus, 5 of arteriosclerosis, 3 of cerebral syphilis, 2 of dementia paralytica, 1 of multiple sclerosis, 1 of trauma, 1 of epilepsy and 1 of epidemic encephalitis. The most characteristic symptoms, although varying from patient to patient, were somnolence, psychic disturbances, lack of interest, stupor or excitement, sphincteric disturbances, disturbance of speech, vomiting, dizziness, headaches, forgetfulness, Korsakoff's symptom, confabulation, gradual loss of eyesight, no feeling of illness, double vision, paralytic symptoms, fluctuation in weight and frequent remission and relapse. On physical examination there were often a sensitiveness to percussion of the skull, unequal or irregular pupils, diminished or no reaction to light in one or both pupils, optic atrophy, a partial or complete pallor of one or both fundi, ptosis, oculomotor paresis, nystagmus, paresis of the arms and legs, etc. Of the severe cases of tumor of the brain, 4 revealed post mortem an involvement of the area near the third ventricle. Of 2 cases of tumor of the hypophysis, 1 came to autopsy, substantiating the clinical diagnosis.

Many of the symptoms are the result of involvement of adjacent areas. Whether the process extends orad or caudad, or as it involves other organs, the symptoms develop correspondingly. Thus some cases show cerebellar symptoms, or optic atrophy appears, or symptoms of involvement of the frontal lobes become manifest. Some of the symptoms are the result of indirect pressure. That Korsakoff's syndrome may be caused by general cerebral injury is admissible. Whether primary or secondary, the interbrain syndrome appears when the local pathologic condition develops. Extrapyramidal disturbances are often present as an expression of involvement of adjacent areas in interbrain disease; also symptoms of involvement of the corpora quadrigemina and connecting cerebellar tracts may be present. General intracranial pressure is often absent in tumors of the stem, except for the alternating hydrocephalus when a ventricle is blocked. Spontaneous remission must depend on cystic tumors or blocking of a ventricle. Stertz explains the lack in his cases of such well known symptoms in disease of the interbrain as diabetes insipidus and dystrophia adiposogenitalis by the possibility that the parts controlling the functions involved in these disturbances have a strong power of resistance, so that even in severe destruction of the interbrain area symptoms of disturbance of these parts do not always appear. In many of the cases reported, however, there were symptoms pointing to disturbances of these areas, such as abnormal thirst, sensation of hunger, fluctuation in weight and general weakness.

Important in the symptom complex is the manifestation of hypofunction or hyperfunction, which probably has its basis in a change from stimulation to paralysis. There can be observed sleeplessness and lethargy, narrowing and dilatation of the pupils, retention and incontinence and an increase or loss of weight. The diminished psychic activity can also be contrasted with an increased psychic activity.

#### SPECIFIC AND NONSPECIFIC TREATMENT OF MENTAL DISEASES. WAGNER-JAUREGG, Vienna, Austria.

Wagner-Jauregg calls attention to the fact that favorable effects of infectious diseases on different disease conditions were observed long ago. This especially engaged the attention of psychiatrists, who began to investigate the therapeutic value of this therapy. In 1887, Wagner-Jauregg published a paper on this subject in which he collected all the information from the literature and suggested the induction of artificial infection in psychic cases, e. g., erysipelas and malarial infection.

As soon as Koch's tuberculin became known, Wagner-Jauregg began to use it in cases of mental disease. Results obtained with tuberculin, as far back as

1895, led him to the assumption that in favorable cases there might have been present some tuberculous lesion, which brought about a reaction with the tuberculin and thus may have been responsible for the favorable results.

This assumption gained support from the observation that the favorable cases were those in which the patients reacted to the injection of tuberculin with a high fever, while cases in which after the injection of tuberculin, even following a rapid increase in the dose, the fever subsided quickly as a rule remained uninfluenced by the treatment.

In the last seven years treatment with tuberculin was again undertaken, not in the old way with strong reactions, but rather with small doses. Cases of schizophrenia which were not of long standing and in which a tuberculous process was present in the lungs or in the hilar glands were selected. Cases in which open tuberculosis were present were excluded. In a few patients a complete cure took place; in others improvement was observed. However, in all cases there was an increase in weight. In these cases treatment with tuberculin may be called specific in so far as one assumes an etiologic relationship between the psychosis and the tuberculous infection. The next question is whether there are not other chronic infections that bear a similar relationship to psychoses, such as streptococcic infections. As a fact, some mental disturbances run parallel with chronic suppurative processes in the tonsils, which makes such a relationship likely. In such cases Wagner-Jauregg obtained success with vaccine or autovaccine treatment. Probably there are other chronic infections that bear an etiologic relationship to psychoses and that could be treated with specific vaccines. The number of patients who can thus be successfully treated with specific therapy may not be many.

On the other hand, within recent years the treatment employed was mainly nonspecific. As a result of the success obtained with malarial treatment in dementia paralytica, the same treatment has been attempted in other psychoses, especially in manic-depressive psychosis and in schizophrenia. Also other methods that bring about a high fever have been tried, such as the injection of typhoid vaccine, a nonspecific protein preparation, sulphur in olive oil and other preparations.

Remissions often occur in these cases without any treatment. In order to learn the value of this method of treatment, Wagner-Jauregg has compared a number of patients with dementia paralytica treated with tuberculin with an equal number not treated with tuberculin; the same has been done with a number of patients with dementia paralytica treated with malaria and an equal number not given this treatment. Similar studies were made of patients treated with malarial fever, with saprophites and with nonspecific protein. The cases were taken in order as the patients were admitted to the hospital. Wagner-Jauregg suggests this form of investigation as the best means of learning the usefulness of the method of treatment.

CASUISTIC CONTRIBUTION TO THE STUDY OF FUNCTIONAL CHANGES IN THE STATO-OPTOSENSORY SYNDROME. VICTOR VON WEIZSÄCKER, Heidelberg, Germany.

In two previous articles, Weizsäcker reported 2 cases that were characterized mainly by a deviation of spatial direction in the optic and motor functions, but at the same time were also beginning to show signs of changes in perception and movements of different parts of organs. The cases reported in this article resemble partly the cases described by Bárány, Goldstein and Reichmann. Hoff and Schilder, Ruffin and Wilder reported cases which substantiate Weizsäcker's observations, so that together with the older observations made by Lenz, Allers and Günter they form a clinical basis on which certain deductions are made possible.

CASE 1.—A man, aged 55, who had always been well and who served in the war in the front line for twenty-eight months, fell and struck the back of his head in July, 1927. He was unconscious for three or four days. After three months he was again up and about. The first attack occurred in November, 1927, as if "a bubble passed through the head;" everything turned around. For hours he had to remain in a sitting position and then for eight days in bed. Two weeks later,

headaches and anxiety developed. He tired easily. Everything he looked at suddenly began to flicker. In walking he always fell to the left. He had a sensation as if the right eye were larger than the left. At times he did not recognize people 70 cm. away from him. Everything appeared in a vertical position and at the left. It was difficult for him to orient himself in the dark. It appeared to him that his left hand, indeed the entire left side of the body, was thinner, smaller and weaker. He drank a great deal. The heart and aorta were enlarged; a slight renal insufficiency was present; the Wassermann reaction of the blood was negative, and roentgenograms failed to show a fracture of the skull. On looking to the left he had a horizontal and rotatory nystagmus. There was visual weakness of the left eye, which could not be explained ophthalmologically. The left visual field was concentrically contracted.

Perimetrically it was found, when proceeding with the examination without a stop, that a typical helicoid contraction developed. If one quadrant alone was stimulated for a long time, visual power diminished in that quadrant.

Later, attacks developed almost nightly with gooseflesh and a feeling of dullness in the left leg or in the back up to the neck and the head; the patient felt as if the neck were larger than the head; then he became dizzy, and everything turned around him alternately to the right and the left. There was anxiety, an impression as if some men of small stature, who he saw indistinctly, came toward him. Observation was good, but memory was poor. There were motor and sensory disturbances on the left side of the body. The deep reflexes on that side were diminished; this was also true of the corneal and conjunctival reflexes. In walking he swayed to the left, especially when the eyes were closed. While sitting, he had ticlike torticollis movements of the head to the left. The right hand was restless, and the head was carried to the left. On the request to raise both arms with the eyes closed, he raised only the right arm, while the left remained at rest. On opening his eyes he looked surprised and then also lifted the left arm. He did not know that it was not raised. When he closed his eyes the left arm sank rapidly. When told to raise the arms sideways with the eyes open, he raised the right arm much higher; he explained that this was because the left arm felt heavier. In walking, he felt as if he had a heavy weight on the back of his head. The Romberg sign was positive; he fell backward; adiadokokinesis was present on the left; there was constant past pointing to the left (8 cm.) with the eyes open; with the eyes closed, it was inconstant. When told, with his eyes open, to touch the right ear with the left hand, he touched the right cheek, and then corrected himself. When he was requested to do the same thing with the eyes closed, the left arm did not move in the least.

The following observations were made in the optic field. While the patient walked with the left eye open, he was shown a rod, 1 meter long, held in various positions. This was seen as follows:

Actual Position	Position as Seen
Vertical.....	Inclined to the left
Inclined to the right.....	Vertical
Horizontal.....	More to the left
More to the right.....	Horizontal

The discrepancy in the experiments reached 10 or 15 degrees. There was definite micropsia in the left eye. To the left eye everything appeared smaller than to the right (about 25 or 50 per cent).

Line Figures: A circle appeared oval. Circular objects of different kinds appeared to rotate counter-clockwise. When shown a cross on a paper, the patient thought that it was turning like a windmill. A straight square appeared to turn sideways. Stereoscopically, when the right eye was shown a square and the left eye a cross, the patient saw a square with a cross in the middle. A vertical rod was shown with alternate covering of the right and the left eye. This gave an impression of a pendulum movement. Looking through a picture book, he remarked, "The wheels of the wagon are turning. Everything appears sideways." Other figures were shown, such as a cross, a square within a circle, a cross

within a square, a circle divided equally into eight, four and two parts and a spiral. Most often he found that the circular part of the figure turned round.

Color Vision: With the right eye he saw normally; with the left eye he was uncertain of the colored objects in the room (tungsten-niter lamp, 40 watts at a distance of 17 cm.; sodium yellow at 2,500 on the ocular tube).

Examination with Nagel's anomaloscope gave the following results: right eye, Rayleigh equivalent, sodium slit 23, mixed red-green slit, 48; left eye, with the same adjustment (23 and 28), no color—completely gray. The Rayleigh equivalent is made up as follows:

Sodium Slit	Mixed Slit	Statement
15-20	30-60	Same color
20-25	70-90	Same color

The adjusting mixed color slit (red-green) from 30 to 90 gives the Rayleigh equivalent. In continuing the examination a condition of the eye develops in which each desired adjustment signifies "equivalent." When the upper mixed slit was covered and, with a maximal light (90), the entire spectrum was permitted to pass, the following answer was obtained:

Scale of Ocular Tube	Answer
2,533.....	Red; one point very green
2,533.....	Yellow-green, lighter
2,572.....	Gray, less light
3,310.....	Gradually disappeared
3,529.....	Nothing
3,429.....	Slightly greenish

The maximum luminosity for this patient was at about the yellow-green, but the ability to distinguish brightness was apparently diminished, and it diminished further during the examination. The same was true for differentiation of colors. It must be assumed that this was caused by a high degree of breaking down of color vision. As in all these cases there appeared at the same time a diminution in ability to distinguish brightness and weakness as regards red-green, a dichromasia in the sense of red-green blindness and finally a monochromasia.

Chronaxia of the eyes was as follows:

	Rheobase	Chronaxia
Right eye.....	10 volts	1.6 seconds
Left eye.....	32 volts	8 seconds
	.....	12 seconds
	34 volts	16 seconds

The chronaxia for optic stimulation was therefore increased in the left eye, and it increased further with the advance. The rheobase was also increased, but did not increase in the course of the examination.

There were sensory disturbances in the distal parts of the left extremities, with summation manifestations and gnostic disturbances; passive movements of the left upper extremity were not well recognized. Disturbances in the sense of weight were present. The entire left extremity felt as if it were different—as if it were smaller, thinner, weaker and heavier. Objects in the left hand appeared smaller than in the right. The circle of a round glass appeared as oval when examined with the left hand. Winking, threatening motions and salutations were slower and uncertain under optic control; restless movements of the fingers disturbed the course. The movement of the left hand in feeling objects was clumsy.

Chronaxia of the sensibility at the left middle finger pad was as follows: rheobase, from 85 to 90 volts; chronaxia, about 4 seconds, rising to 8 seconds during the examination.

CASE 2.—A man, aged 37, had erysipelas in 1925, with disturbance of the right knee. After 1927, he complained of increasing tiredness and exhaustion, and lost 30 pounds (13.6 Kg.) in weight. At that time there was nothing abnormal on examination of the cerebrospinal fluid and the nervous system. Then headaches, dizziness and vomiting suddenly developed. After a period of excitement he became

dizzy and fell down one step unconscious. After that he suffered from headaches and a constant pressure in the right parietal area. In walking he tended to sway to the right. When he was dizzy, everything turned to the right. It appeared to him as if his feet had grown larger. An examination in January, 1928, revealed, among other things, that he tended to fall to the right and that he past pointed with the right finger to the right. The sella was somewhat large, but during many months remained unchanged. There were not sufficient findings for assuming a pituitary disease. The visual fields were normal. A few months later, sensory disturbances appeared in the right hand and also weakness in the right extremities. There was hyperesthesia in the area of the right trigeminus. At close vision there was a divergence of less than 1 degree. Stereoscopic vision was normal. Repeated examination of the ocular muscles with the Maddox rod showed no gross abnormality.

In April, 1928, the hypesthesia of the right side of the body increased; there were ataxia in the right leg and diminished power in the right extremities. A positive Romberg sign appeared for the first time, and the past pointing of the right hand to the right was 10 cm. At this time hysterical manifestations appeared.

With both eyes objects appeared higher on the right than on the left eye. With the right eye alone they were seen toward the right and were nearer and larger. With the left eye the impression was normal in all directions.

The impression of the position of surrounding objects in relation to the gravity of the earth did not conform to the impression of the direction of a rod, which

#### *Tests of Visual Perception*

Objects	Binocular	Right-Sided Perception
Horizontal.....	Right end deeper and nearer	Left end deeper and nearer (more marked than with both eyes)
Vertical.....	Upper end tending to move to right	Upper end tending to move to left (more marked than with both eyes)

perhaps did not appear as a body of distinctly three dimensions. The impression of written figures was not normal. A square appeared as a rhombus, and at times a cross appeared also as a rhombus. There was normal vision in the left eye, but not in the right eye. Stereoscopic vision was nearly the same as binocular. With the left eye a circle appeared normal; with the right eye it appeared as a flat oval and in clockwise rotation. The right side of a circle appeared heavier, and sections of the circle were lost (*Gestaltzerfall* or form crumbling). With binocular vision there also developed a clockwise rotation and crumbling. At times with monocular vision diplopia or triplopia developed. Perpendicular chalk lines on a blackboard gave the impression of being bent in many places. In general there was a tendency to see objects with the right eye in motion, to rotate round objects and to press together many figures in the visual field, up to a fusion point, or to cover them. The phenomena are similar to those described in case 1.

This patient had also diminished color vision in the right eye. Yellow appeared lighter and more white to the right eye than to the left; on the other hand, red and blue appeared much darker to the right eye. With the right eye he was unable to separate mixed color points and to count them.

Moving after-images were easily developed in the right eye. Colored after-images, on the other hand, were less impressive with the right eye than with the left.

Duration of after-images and Talbot's fusion frequency were partly tested with a rotated electric lamp and partly with the black-white sector disk. In general, the relation was found to be about 4:3; that is, in the right eye the fusion of successive impressions appeared at a slower frequency. On repeated examination of the right eye, fusion appeared more easily, and the rotated red lamp appeared to be a constantly narrowing spiral.

Sensibility: Aside from tactile disturbances, there was a tendency to over-estimate weights, especially on repeated long examinations. The round weight in

the right hand appeared larger; the same was true of lines marked on the skin. Intervals between successive stimulations of the skin appeared shorter in the right hand than in the left.

The patient also had a sensation that the right arm was longer and heavier than the left. No such distinctions were felt in the legs.

Motor power (with eyes closed): When told to hold a rod in the right hand in a vertical position, the patient held it toward the left and in front. When told to hold the rod in both hands in a horizontal position, the right end remained 5 cm. lower than the left. When he was told to hold the rod in the right hand in a horizontal position, the right end was lowered 12 cm.; under the same test with the left hand, it was lowered only 2 cm.

When both arms were slowly raised forward or sideways, the right arm remained behind. In holding both arms for some time in a horizontal position, the right arm was quickly lowered; there was a loss of tonus. In holding the arms obliquely to the right and left, the right was slower in reaching the midline; in strong supination of the hands the right hand yielded in half supination (Schilder's phenomenon).

Symptomatically, both cases as well as cases previously reported showed the syndrome which Goldstein and Reichmann described as the "symptomatology of cerebellar disease." The cases described here showed on the one hand a motor and optic systematic disturbance of direction, and on the other hand a unilateral disturbance of the sense of weight, space and time perception. While von Weizsäcker attempted to obtain an explanation and unity of these systemic geometric disturbances from spatial constructive functions of verticality, horizontality, etc., Goldstein and Reichmann considered the problem from the point of view of muscle tonus and the reflex or reaction time. In case 1, the left vestibular organ was apparently diseased; Goldstein in his cases assumed a cerebellar disturbance. Hoff and Schilder likewise assumed vestibular disturbance in their cases. A strict organic symptomatic diagnosis points to a disturbance in both of the illustrative cases, and indicates that the localization—the reference of all the manifestations to a definite focus—is most doubtful.

As long as a neurologic diagnosis limits itself to reflexes, motor and sensory disturbances, one may take the liberty of speaking of reflex function, motor and sensory function or centers. A very simple technic of examination presupposes a very simple idea of function. But the untenability of this conception becomes at once apparent when the methods of examination are greatly extended, and the organism is considered from points of view that were not thought of before. Then the problem arises: What does one understand by "a function," and what are the elementary functions from which all others develop? Are such functions definitely established? Conceptions such as reflex, tonus and threshold are no longer self-explanatory, but have become rather problems.

From this point of view one is able to recognize in an organ such as the eye, the skin or an arm a large variety of tasks, with a formal collectivity of all such functions, especially the pathologic in relation to the normal. In a review of the activity produced, one will not limit it to elementary functions or to its losses. While formerly symptoms were observed, pathologico-anatomic findings were advanced for their interpretation, and eventually this was substantiated by animal experimentation, the time has come when a qualitative and quantitative all-embracing functional test is to be undertaken, so that the physiologic and psychophysical processes in the altered organism and not merely lost functions can be observed.

Such a study will appear the more important when a syndrome is present the unity of which is conceived less as a local than as a functional principle. In this respect von Weizsäcker observes that his cases at first presented great difficulties, since they manifested neither a local nor a functional unity. But some advance has been made by the author in this direction. It is to be remembered that in all these cases there is present a "vestibulo-cerebellar" complex,

coupled with an "optic" complex, and in a few of the cases this vestibulocerebello-optic complex is further expanded in the sphere of sensory perception. The localization presents difficulties in different directions: (1) The aforementioned three or four functional areas cannot occur topographically in one known area of the brain; (2) the individual symptoms are partly identical, but are partly different entirely from those customarily observed in lesions of the visual tract or in sensory or vestibular lesions, peripheral or central; (3) a syndrome is present which runs contrary to all ordinary conceptions concerning the coordination of structure and function, namely, monocular-agnostic or dysgnostic disturbances.

The fact that in some of the cases there is a monocular breaking up of perception, without any reason for assuming the presence of a lesion in the eye itself and in the visual tracts, including the calcarine region, is a many-sided paradox. On the one hand, like Liepmann's unilateral apraxia, this type gives the impression of being due generally to such factors as confusion, lack of attention and fatigue, circumscribed and organologically bound together. Further, there can be observed a gradual breaking up of optic perception to a completely agnostic state, and although its basis is neither hemiopic oculomotor, oculosensory or refractory, it may involve one eye, leaving the other undisturbed. Such a condition can be understood only when there is present a cerebral physiologic representation of vision with one eye. However, since the innervation of the internal and external ocular muscles, as well as the sensory excitability of the entire visual field, were found undisturbed in the reported cases, neither the "motor" nor the "sensory" nor even the "gnostic," disturbance in the sense of Wernicke can serve as an explanation. The assumption of a special type function such as Hering designated as attention will lead one much farther afield: a physiologically understood function, which at times is more motor, at times more volitional, but always essentially associated with the structure of apperception. J. Stein called it "sensory motion." With this assumption there enters between the processes of the retina and calcarine cortex, on the one hand, and the ocular muscle centers and the ocular muscles, on the other, a new functional niveau, the conception of which is that the left and right visual fields are separable; otherwise the monocular diseases would be impossible.

The cases described here show that the functional breaking-up from this functional niveau does not stop with the apperception of the spatial structure. With the progressive breaking up of the spatial apperception structure of tendencies, distortions of reversion to a primitive form and marked lapses of impression of rest and movement up to the point of agnosia there is also a breaking up of the sensation of light and color. It affects visual power in all particulars. The functional separation of the motor and sensory functions of spatial perception and the types of the principal perceptions as they are conveyed in classic physiology appears here to be especially questioned. If these considerations are correct, a pathologic type of breaking up appears which especially enables one to gain insight into the functional fields of the transmotor and the transsensory strata.

To recapitulate the most important manifestations, they are: (1) spatial structure, tendencies, rhombic and elliptic distortions, micropsia, macropsia, primitivization of form with a preference for retaining orthogonal, parallel and vertical directions, tendency to form (*Gestalt*) crumbling, movement and certain rotation of lights; (2) breaking up of light and color from red-green blindness up to achromasia; weakness of after-images, increased Talbot's fusion, rapid fatigue of local sensitiveness and raising of chronaxia (lability).

Of special theoretical importance is the connecting of these many diverse partial functional disturbances. When the question is raised whether a functional principle can be discovered in these three groups, the answer always leads to the process of nervous excitability. This process has a phasic character: a slower or faster course and, in connection with this, a different frequency. Therefore there is a possibility of developing, on the one hand, a pathologic velocity and, on the other hand, a pathologic frequency. If it is assumed that in the breaking up there is a decrease in the rapidity of the flow of the stimulus as well as a variability

of frequency, these purely formal changes in the analysis of optic function must appear unmistakable in effect. In the cases reported, many observations were pointed out that indicate a delay in the flow of the stimulus, such as the rise in chronaxia and the increased fusion.

On this point the following observation is of interest. The patient in case 2 was made to observe binocularly in a frontal plane a moving pendulum. 1. With a yellow lens before the right eye he saw an ellipse which was nearing a circle. 2. With a yellow lens before the left eye, he saw a flat ellipse. 3. With a gray lens before the left eye, he saw it swing nearly in one plane. 4. With uncovered eyes, he saw a flat ellipse.

According to Pulfrich and Kries, in these cases the light stimulus strikes one retina with less intensity than it does the other. If it is assumed that the transmission of the stimulus in the more weakly stimulated eye is also slower in developing, the stimuli do not strike simultaneous identical places at the point of binocular union, whereby the spatial phenomena take place. This can be observed in a normal person by placing a gray or yellow lens before one eye. The patients in the cases reported showed this even without the addition of a lens; by the addition of a lens it became intensified or compensated according to whether the lens was placed before the affected or the normal eye. According to this theory, the conclusion is to be drawn that on the affected side there is a delay in transmission of the stimulus. The disturbance of color vision could be attributed to the same cause.

The question is raised as to whether the characteristic tendencies and distortions in the visual field can be attributed to a similar formal change in the activities of the stimulus. An example can here be offered to show how the factor of the time of the neurophysiologic stimulus is transferred into perception of a spatial character. The hypothesis is here permitted that the seeing of a vertical line is the result of a right-sided and left-sided dynamic movement, just as the drawing of a vertical line is brought about by a dynamic evenness of muscular motor power of abduction and adduction of the arm. Comparing the condition of muscle antagonism and its dynamic effect with the physiologic occurrence of the impression on seeing a vertical line, it becomes understandable that the ordinary vertical line must have a tendency to be seen toward the left when the impulse of the left side of this optodynamic combination is somewhat delayed or weak. In fact, with this hypothesis it is also possible to understand the striking systematic spatial disturbances as a unified fundamental disturbance of the physiologic stimulus, especially as relates to time. Micropsia and macropsia can be explained similarly, since the impression of absolute size must be similarly the result of a dynamic combination of the uneven course in time of the stimulus. However, at present this cannot be put forth as a systematic theory; it is so far merely in the realm of thought. But the conception also offers a basis for the analysis of the motor-tonic and sensory syndrome, since here too the observation is the same: deviation of verticality and of sagittality, manifestations that appear smaller or larger, lighter or heavier in weight, etc.

So far no case has been reported with observations at autopsy. Goldstein and Reichmann considered the symptoms of the reported cases as being due to cerebellar disturbance. This is not surprising when one considers the then prevailing knowledge, but it must be admitted that ordinarily the cerebellum does not produce such symptoms, and that some of the cases reported did not show definite or exclusive cerebellar lesions. The first case reported here was one of trauma. Günther's patient had a cerebellar abscess. Von Weizsäcker reports a similar case in a man, aged 74, with visual manifestations. Autopsy showed a discoloration of the left inferior temporal gyrus, with perivascular infiltration; the brain was small; the left side of the cerebellar substance was discolored; a blood vessel, 1 mm. in diameter, was found closed, and there was a diffuse softening of the white substance of the area with accumulation of fat granular cells. General arteriosclerosis was present.

The observation of slanting vision in a case of unilateral cerebellar softening again points to the cerebellum as in the case of Günther. But the objection here is the senility of the patient.

The observations cited speak for the fact that there is a physiologic breaking up of a specific functional area, and that it is no longer correct to speak of focal or localized diseases but rather of functional diseases. Undoubtedly the functional diseases in certain respects are organically associated; the vestibulocerebellar, the optic, the tactile and the tonic-motor areas are more or less definitely stressed. But all these areas do not take part as in local lesions. The impression is gained rather that behind the organ apparatus the functional layer which is combined with it is affected: a meta-organic functional area, as described in the optic disturbances.

BERNIS, Rochester, N. Y.

## Society Transactions

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### NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

*Dec. 13, 1932*

BYRON STOOKEY, M.D., *Chairman*

#### CONDITIONED REFLEX IN RELATION TO PSYCHOANALYTIC TECHNIC. DR. LAWRENCE S. KUBIE.

Quoting from Pavlov, it may be pointed out that a focus of strong excitation can give rise to a generalized inhibition, that under such circumstances important unconscious chains of associative connections can be set up in the inhibited field, and that it requires special conditions for these inhibited or unconscious associations to emerge from the unconscious into the conscious field. This communication attempts to demonstrate that the psychoanalytic method meets the requirements of these special conditions as they are implicitly indicated in the experimental work of Pavlov.

It may be pointed out first that the cerebral cortex is under constant stimulation, not only toward activity, but also in the direction of inhibition, with the result that in order to secure a maximum amount of spontaneous cortical activity it is necessary to reduce to a minimum the mass of incoming stimulation. For this reason, the passive restraint of the analyst is found to be more "disinhibiting" than any more active approach to the patient could be. This aspect of analytic technic, therefore, is precisely designed to reduce "external inhibitions."

Second, it is clear that with the reduction of external inhibition and the use of free association each unit in the free association becomes an element in an intricate mosaic of conditioned reflexes, one interrelated with another and all of them interweaving in and out of the fields of excitation and inhibition. In this way the patient is inevitably led through the inhibited or unconscious fields in the course of his work.

Third, the analyst's attitude toward time relationships in cerebral functioning is essentially the same as that which has been experimentally demonstrated in the work on conditioned reflexes. The analyst makes the tacit assumption that if two ideas appear in a patient's mind in a definite sequence or relationship in time, even if there is no superficially recognizable logical relationship between these ideas, nevertheless the mere fact that they appear together is evidence that there must be some dynamic relationship between them. This is a converse of the experimentally demonstrated fact that if two influences impinge on the nervous system with no other relationship than that of time, they will, for this reason alone, set up an intimate connection within the nervous system. It is this temporal relationship between ideas and feelings which is used by the analyst in his investigation of the patient's free association.

Pavlov's growing realization of the importance of variations in instinctual tension supports the analyst's attitude toward that reservoir of instinctual tension which he calls the "libido" and further justifies the analyst's dictum that an analysis must be conducted under deprivation. The physiologist has found that in the absence of instinctual tension no conditioned reflexes can be established, and that with satiation both conditioned and unconditioned reflexes become inhibited. The analyst must, therefore, refuse gratification to the patient in order to avoid blanketing the unconscious syntheses under inhibition.

In conclusion, therefore, it seems that the analyst who remains a passive observer, who avoids all external stimulation of the patient, who strives always to facilitate the patient's free flow of unguided speech and who reduces to a minimum the patient's gratification in the analysis is actually conducting a procedure which is approximately a mirror image of a classic experiment on the conditioned reflex, conducted through the medium of spoken language.

TURNING POINTS IN THE ANALYSIS OF A CASE OF ALCOHOLISM. DR. GEORGE E. DANIELS (by invitation).

This paper contrasts, by means of a clinical example, the method of arbitrary limitation of the consumption of alcohol, with gradual analysis of the factors to a point where the patient can be induced to accept his share of responsibility for the treatment. The rest of the material in the analysis has been subordinated to this one point.

The patient, a single man, aged 30, a college graduate who had made a good superficial adjustment, up to the time of and during the analysis had held a responsible position. He was overtly bisexual, but during the period of initial symptoms gave up the heterosexual object. Though the patient was subject to occasional depressions and drinking bouts, there were no serious symptoms until the death of a sister two years before the analysis began. With the onset of symptoms he became depressed and began to drink heavily; this continued daily almost without interruption. The amount of liquor consumed varied from a pint a week at the beginning of the analysis to a quart a day, which he had consumed during a two months' period a year before. Nine months before commencing treatment he experienced a severe outbreak of anxiety, of which there were occasional recurrences. It was these attacks which finally drove the patient to seek treatment, as he feared that an organic disintegration had set in. There were no physical signs of organic change, however, and the anxiety proved to have a definite oral conditioning.

The patient's hostility toward any interference with his drinking, combined with a history of extreme violence as a child when crossed, made it important to move cautiously and gradually in order to win the patient's cooperation in dealing with the outstanding symptom of the neurosis. Gradually a lukewarm, conscious desire to limit the liquor appeared, without, however, his making any progress in its control. It was evident that besides analysis of the drinking, it was necessary to obtain a positive attitude toward the problem without requiring a definite commitment from the patient, which the analysis showed would have been utilized as resistance. This was linked clearly with an early conflict over masturbation, when he had decided that he would either have to give up masturbation or confession, and had given up the latter. The inference in relation to the analysis was clear.

The attainment of the desired attitude occurred rather dramatically after five months. It was preceded by a sharp increase in the drinking and a return of anxiety for a few days. The accompanying intrapsychic struggle was registered in a significant dream, showing the acceptance of his share of responsibility in the treatment, beneath which was acceptance of responsibility for his genitality and courage to recognize his own penis. Following this a striking improvement occurred in which continuous drinking was replaced by sporadic recurrences. These threw the conflicts into relief so that they could be analyzed individually. The change was followed by another a month and a half later, when the homosexual attitude became colored by definite heterosexual strivings. This latter situation was also epitomized in a dream.

PSYCHOANALYTIC POINT OF VIEW OF DRUG ADDICTION. DR. SANDOR RADÓ (by invitation).

I regard drug addictions, including alcoholism, as varieties of a unitary psychic disorder, for which I propose the name "pharmacothymia." In pharmacothymia,

the ego renounces the "realistic regimen" and sets for itself the task of regulating its self-regard and its mood with the aid of "pharmacogenic pleasure." Because of this pleasure, the libido is diverted from genital and extragenital utilization. The patient renounces sexual and social activity. The throttling of the ego's vitality intensifies, by reaction, the instinctual force of masochism, which is antagonistic to the ego. The clinical course is characterized by a periodic alternation of "pharmacogenic elation" and "pharmacogenic depression," and the phenomenon of "diminution in elation," which ultimately leads to a crisis. The crisis may terminate in three ways: (1) flight into a free interval, (2) suicide and (3) a psychotic episode. The symptoms appearing then are determined by the collapse of the elation (or anxiety function) and by the eruption of masochism, and can be understood as derivatives of these antecedents. Insight into these relations leads to a new conception of homosexuality and of certain other sexual disturbances that are characteristic of pharmacothymia.

#### DISCUSSION ON PAPERS BY KUBIE, DANIELS AND RADÓ

DR. A. A. BRILL: Dr. Kubie's paper recalled to me the time when, in the clinic of psychiatry at Burghölzli, we experimented in order to test the validity of Freud's theories experimentally. Everything that Dr. Kubie has said in reference to Pavlov's conditioned reflex was demonstrated in the association experiments. In fact, that was the main reason why Bleuler, who was the first to sense the value of Freud's work, became convinced that Freud had given new life to psychopathology. As he put it, "Without Freud there would be no psychopathology." The mechanisms of Pavlov's conditioned reflexes can in a way also be demonstrated in the association experiments, particularly if one uses the galvanometer in conjunction with the association experiments. The test person and the patient saw nothing of the experiment—the galvanometer was in a different room—but the emotional curves invariably corresponded to the complex indicators of the association experiments.

It is impossible to discuss all the points that were brought out by Dr. Daniels and Dr. Radó. Dr. Radó gave me for the first time a clear and lucid psychoanalytic presentation of the subject. I am particularly interested in the relation of drug addiction to the oral zone. In 1919, the Academy of Medicine held a symposium on the subject of alcoholism, just when prohibition was being put into effect. Five of us were asked to speak on the various phases of alcoholism. I believe that Dr. Jelliffe was one of the speakers. Up to that time I had paid slight attention to the deeper mechanisms of alcoholism. If I recall rightly, there was only one paper on alcohol, which was by Dr. Karl Abrahams; he showed that alcohol, by removing inhibitions, brings to the surface the homosexual component in man. In my paper I reported the case of a man, who, when he stopped drinking, had attacks of excessive eating; he had what he called "eating jags." In the same paper I reported similar cases in which there was a distinct association between the oral phase of development and alcoholism. When I first encountered these cases I could not quite understand them, but as I learned more about oral organization as a pregenital development it became plain that there were regressions to the early oral organization. Even in normal life, when people wish to reduce tension, when they are under stress, they regress to oral outlets; they drink, chew or smoke. The same has been observed among primitive people. Leo Muller, an ornithologist, in describing his experiences with South American Indians, made the statement that when they carried heavy weights in the grueling heat of the jungle, they continually chewed coca leaves. In the Far East people chew betel nuts, just as tobacco and chewing gum are used in this country. I read recently that in the United States in one year about \$30,000,000 is spent for chewing gum. Resort is made to chewing to get a pleasure outlet through the oral zone or to reduce the tension occasioned by the stress of life. That is the only point I wish to bring out in discussion. Psychoanalysis teaches that every infantile organization may be subject to some injury or trauma to which the subject may later regress. There is no question that in drug addictions there is an oral regression.

It is significant that a great many so-called poets, the masters of words and diction, have also been drug addicts and have had alcoholism.

Dr. Radó gave an excellent explanation of the evaluation of the various phases of alcoholism. There is one phase, however, which he did not mention; when he closes the discussion I wish he would say something about the so-called alcoholic delusions of jealousy (*Alkohol Eifersuchtswahn*). At a state hospital I had two cases of alcoholism which puzzled me. One was that of a physician, a periodic drinker, who told me that he had found out accidentally that he could avert a periodic attack of alcoholism by resorting to a sexual debauch. I could not find any explanation for this substitution, which psychoanalytically means resorting to object libido instead of oral libido. At the time I did not think that the sexual attacks had anything to do with the alcoholism. Another case was that of a Jewish patient who presented a very extreme case of delusions of jealousy, but he was not alcoholic. His wife, who sent him to the hospital because of his insane jealousy, was convinced that he did not drink. After considerable investigation I found that he suffered from a relative sexual impotence, and I concluded that this was the reason for his jealousy. He repressed his sexual weakness and blamed his wife for it. But the patient's delusions or morbid fantasies of his wife's sexual behavior with many men of a certain type showed plainly that he identified himself with her and thus lived through his repressed homosexuality. When one goes into the deeper processes of such patients, one can readily see the close association of alcohol, drugs and pregenital sexuality; as was shown so clearly by Dr. Daniels and Dr. Radó, it is not primarily a question of alcohol or drugs, but of the whole evolution of the personality.

DR. GEORGE W. HENRY: When Dr. Oberndorf invited me to comment on Dr. Radó's paper, he mentioned that he would like to have someone who is somewhat critical of psychoanalysis. I should modify that statement a little in this way: I am inclined to be somewhat critical of psychoanalysts and their methods of applying psychoanalysis. There is a difference. I wonder why it is that in a meeting of this kind someone who is not an analyst is usually invited to criticize psychoanalytic papers. How is it that that happens so often? Why do the psychoanalysts not criticize their own presentations? Some years ago I had the pleasure of listening to Dr. Radó in Berlin while he was giving a series of lectures, and I am satisfied that whatever he has to present merits serious consideration.

First, let me comment on the general attitude, since it is somewhat typical of the attitude of psychoanalysts, especially in regard to psychiatrists. In the early part of the paper is the following statement: "The psychoanalytic study of the problem of addiction begins with the recognition of the fact that not the toxic agent but the impulse to use it makes an addict of a given individual." A little before this Dr. Radó says: "Psychiatry is wedded to the idea that drug addiction is a somatic intoxication, the injurious effects of the poison on the brain." He refers to this as a theory of the psychiatrists. I presume Dr. Radó meant to say that it was a fact accepted not only by psychiatrists but by others. He says the same thing later in his paper.

Dr. Radó says that "as far as the question of the susceptibility of the individual to develop a craving for drugs . . . one is groping in the dark." He also says that in psychiatry the idea was promulgated that in a certain type of "psychopathic," "weak-willed" or "uninhibited individual" the desire for these drugs happens to develop. I get the impression that Dr. Radó must be talking about what the psychiatrists wrote at the end of the nineteenth century. Furthermore, he gives the impression that he is going to tell about the sort of person who has an impulse to take drugs. As a matter of fact, nothing is said about that in the paper he has read. He chides psychiatrists for this neglect, but does not give them credit for calling attention to the psychopathic, weak-willed and uninhibited type of person who takes to drugs. What practical difference is there between them and what the psychoanalyst now calls the neurotic person? It is obvious that the psychiatrist long ago realized that there was something which antedated the taking of the drug. Since the psychoanalyst likes to criticize

psychiatry every time he gets a chance, is modern psychiatry any older than psychoanalysis? How does it happen that psychiatrists have long ago called attention to the psychopathic person as being prone to drug addiction, while it is only tonight that Dr. Radó mentions this type of person? Why are psychoanalysts so late in mentioning him? It is exceedingly rare that the psychiatrist is consulted before the patient has become addicted to the use of a drug. Does Dr. Radó mean to suggest that the psychoanalyst can predict who will become a drug addict? It seems obvious that the drug addict still has his neurosis. What is the experience of the psychoanalyst in treating this neurosis and thereby removing the need for the drug?

Dr. Radó says that with the adoption of the psychogenic standpoint the emphasis shifts from the manifoldness of the drugs used to the singleness of the impulse which underlies the craving. Does he mean by that that there is a certain type of personality, a certain type of personality disorder or a certain type of neurosis in which the cravings are satisfied by drugs only? At least he says that all types of cravings for drugs are one disease. He says, "To crystallize this theory, let me introduce the term *pharmacothymia*." Of course, giving a name to something does not add to knowledge. Does the person take drugs for pleasure or chiefly for relief of distress? Again, "*pharmacothymia* originates from tense depression, the result of real frustration. A certain group of human beings respond to frustration in life with a special type of reaction which might be designated *tense depression*." One might ask, what are the characteristics of this group? What is meant by a "real frustration"? If a patient is given morphine by a physician for pain and a habit is formed, is the cause of the addiction in that case a "real frustration"? What proportion of well adjusted persons who were given morphine for a long time for the relief of pain would not acquire a craving for the drug? Or is it only neurotic persons who succumb to the desire for drugs?

Dr. Radó says, "After taking the drug, the ego is augmented to gigantic dimensions, and when the effects are worn off the ego is shriveled together." It seems that these statements are slightly exaggerated. He goes on with, "Now there is in addition a sense of guilt and an increased fear of reality." Pharmacologists have demonstrated pretty clearly that if a dog is given morphine over a considerable period of time, the dog, like the human being, requires larger doses to get the same effects later on. Would Dr. Radó say that the dog was troubled by a sense of guilt and that he had a fear of reality, or would he say, as I am inclined to say, that the chief problem is a physiologic one?

Dr. Radó states, "The *pharmacothymic régime* has a definite course and increasingly restricts the ego's action. This régime is interested in only one problem—depression, and in only one method of attacking it—the administration of the drug. The *pharmacothymic régime* takes the place of the realistic régime." I can see no difference whatever between this description and the one found in any textbook or wherever drug addiction is described, except that psychoanalytic terminology is used.

The only patient mentioned in the course of this paper is the one who told Dr. Radó that "nothing can happen to me." This is sufficient to explain to Dr. Radó why the patient did not stop taking the drug. He says that "the elation has reactivated his belief in his invulnerability. . ." By the time drug addiction is established, I think that it more often happens that there is very little elation, and that the patient is really driven to taking the drug for relief of the discomfort. Dr. Radó himself says that the drug finally fails to provide elation; the regimen fails, and there is what he calls a *pharmacothymic crisis*. In the more advanced cases symptoms appear which are the result of cerebral damage and which are to be interpreted as those of organic disease. In this connection "somatic invasion" is mentioned. Somatic invasion by what? I suppose Dr. Radó means the effect of the toxic action of the drug. In any case, what is added by the psychoanalytic phrase "somatic invasion"?

Dr. Radó describes the relative advantages to the ego of homosexuality and masochism. If the ego in *pharmacothymia* or after withdrawal of the drug accepts

homosexuality, it must be regarded as an attempt at autotherapy. That is what Dr. Radó said in 1932. In 1931, he stated that the ego sought an alimentary orgasm because of its inability to achieve a genital orgasm (*Psychoanalyt. Rev.* 18:69, 1931). Have his views changed in the meantime? Dr. Radó says, "These views seem to me to solve finally the problem of the relationship between pharmacothymia and homosexuality." I should say that these views represent only the first steps taken in attacking this problem, and that however long Dr. Radó lives he will never reach a final solution of the problem.

It is evident that Dr. Radó is occupied with a purely theoretical discussion of the subject. With regard to the personality problem before the drug is taken, for the neglect of which he tasks the psychiatrist, he is strangely silent. Dr. Radó has given an excellent review and description of the course of events after a person has taken drugs, a description which is not different from that already known to us, except that it is phrased in psychoanalytic terminology. As far as the psychiatrist is concerned, the description would be improved if a good deal of the psychoanalytic language were omitted.

DR. SMITH ELY JELLIFFE: I am gratified to have heard Dr. Kubie's thoughts on the relation of psychoanalysis to the conditioned reflexes. Ever since Bechterew produced his interesting objective psychology based on the Pavlov experiments, I have had a belief that there was something missing. I have believed for some time that the psychoanalytic method, properly carried out, is an experimental method that has certain similarities with the conditioned reflex method but has the great advantage that as lower animals can give no indications of what identification mechanisms are operating through displacement, condensation or projection, experiments on man constantly offer checks on interpretation lacking in experiments on lower animals. Thus, much of the interpretation of experimentation on the behavior of animals, instead of being objective, is largely subjective, projection on the part of the experimenter. I shall say no more, as I know Dr. Schilder has done definite experimental work along these lines.

Nor shall I linger with Dr. Daniels' valuable case history. I can say only that my general experience with patients with confirmed alcoholism, using this term in its large sense, has been far from satisfactory. I have come to a time in life when I do not care to be bothered by this type of pharmacothymia. I am willing that the enthusiasms of youth should take up the burden and am indebted to Dr. Daniels for an illuminating case history.

I need hardly remind you that science develops largely on the basis of the peeping tendencies of mankind. Undoubtedly psychoanalysis is the arch soul-peeper. As an ancestral Jelliffe, in the seventeenth century, came from Coventry, the hereditary "peeping Tom" in me can possibly be understood. As a youth I "peeped and botanized" not on my mother's grave, as the poet once spoke, but largely in the old Quaker Cemetery in Prospect Park in Brooklyn. This with chemical peeping afforded the foundation for a great interest in materia medica during my student days, and later as professor of pharmacognosy and also as lecturer in materia medica at Columbia after my graduation and *Wanderjahr*, I kept peeping into the structure and function of drugs. This provided me and my growing family with bread and butter for about ten years. Thus Lewin's "Nebenwirkung der Arzneimittellehre" and related pharmacologic studies were of deep interest. Not only had I peeped into the structure of the roots, the alkaloids, alcohols, ethers, derivatives and synthetics, but, strange to relate, in the preparation of my lectures I had the curiosity and courage to learn first hand about the actions of drugs. I was, however, more Scotch than Irish in temperament in these matters and, having acquired the idea of the action of a drug on my own person, I was willing to let it go at that. It was not difficult to realize that I was vulnerable and had a healthy respect for any traces of false omnipotence. Croton oil will demonstrate this. Furthermore, I never told anybody or boasted about it. I peeped in my earlier days, but exhibit only in my dotage. So when practice commenced to grow and psychiatric interests forged themselves more and more into the picture, it was inevitable that I run into the drug habitué. This was years

before I even had an inkling of psychoanalysis. These experiences, which were of much interest and of intellectual and emotional rather than of pecuniary profit, gave me increased psychologic knowledge, but chiefly brought me into emphatic relations with a certain ecologic horizon of mankind in which policemen more or less move and have their being. Thus to pharmacology and psychiatry was added a full series of contacts with the lower world of the drug habitué, the crook, the prostitute, the invert and the pervert. Having saved the life of one influential heroin habitué from a suicidal impulse, and, as alienist, extricated the wife of a famous gambler from a kleptomaniac debacle, I had free entrée to certain underworld strata of New York, where I can assure you I was even more cannily Scotch than ever and warily watched my step. I looked but knew my place. I soon learned that that was no place for a serious student of psychiatry. It was tragic, dangerous and, what was equally important, highly consuming of time and unsatisfactory of results at restitution, as Dr. Radó points out in his excellent characterization. "The Ego lives in a period of pseudo prosperity and is not aware that it has played into the hands of its own self destruction. The Ego in every neurosis is driven into harmful complications by its masochism; but the pharmacothymic régime is assuredly the most hopeless method of combating it." In this I am in complete agreement with Dr. Radó. Furthermore, the contacts were extremely meager and precarious as to economic returns unless one pandered.

I abandoned this type of contact entirely, but with increasing experience in psychoanalysis I found I already knew much that it later taught me, but from a different point of view. I had gained much from the method of *Einfühlung* as one of the approaches to a *Geisteswissenschaft*. When the deeper insight afforded by psychoanalysis became available I found a fairly full background of clinical and psychologic data with which to work and at one time planned and started with Dr. Pearce Bailey, but never completed, a mass attack on the heroin habitué. I have reams of dreams of 100 or more such patients in various stages of partial decipherment.

Hence my interest in the papers on drugs presented has been deep, and I am indebted greatly to both presentations. There is something intrinsic and basic in practically all of the narcotic group reactions, although it must be borne in mind that, as Dr. Radó has pointed out in a previous study, the toxic equation or idiosyncrasy of Lewin is of great significance. In the first place, to estimate the picture properly, it is of definite value to have some knowledge of the anatomic pattern disturbance. There is no time to enter into details as to the principally cortical readjustment of libido economics in the alcohol group, nor can one enter into the hypothalamic and interbrain participations of the urea derivatives, the phenobarbital, barbitol sodium and the related groups. Nor can I stop to discuss the possible thalamic schisms of the hashish and mescal types of anatomic pattern modification. Fascinating as all of these aperçus may be, the working out of the mental system economics is of the most practical importance, and the papers of the evening have demonstrated certain features of outstanding significance. Here the rapprochement of pharmacanalysis is a fascinating new method of both psychologic and pharmacologic moment.

Primarily the organization of the character becomes subject to fine dissection. This is illy described behind the older pharmacologic criteria of idiosyncrasies. Even the oldest of wise cracks—in *vino veritas*—is seen to be but a half truth after all. Hence there is a special value in the metapsychologic analysis of the phenomena, even though this is not as uniform as one might wish. Most is known about the alcohol group, less about the morphine group, and there are only beginnings of insight into the hashish and mescal patterns, with their rich possibilities of projection. The almost specialized use of cocaine among inverts—although this is a loose generalization—is of significance. I am excluding the southern Negro and his predilections for cocaine as out of my special ken. I need hardly stress the importance of separating sporadic, episodic situations from those showing prolonged habitual use. Here I might hold a brief for the essentially

valuable social aid of sporadic alcoholic indulgence. One should not forget to state, on the other hand, that complications of much significance arise from induced structural alterations, as in the alcoholic hallucinosis and Korsakoff psychosis, as Dr. Radó has pointed out.

Drugs, particularly those of the morphine group, as emphasized, afford internal barriers against stimuli. The thresholds in certain afferent paths are raised, and new dynamic adjustments follow. Radó has well emphasized the strengthening of the ego function. Sometimes this is called "Dutch courage," although there are enormous differences between the type of strengthening of the ego function from alcohol and from morphine.

I can but fragmentarily take up the masochistic situation. It is accurately portrayed, as is also the lessening of genital cathexis and the regression to homosexuality, overt as well as latent. There is no question as to the working of the death instinct, which causes so many pharmacothymias to end in suicide. Dr. Radó's formulation is indeed ingenious. These persons do not die, they live forever.

I am particularly intrigued with Dr. Rado's outlining of the general psychogenic view of withdrawal symptoms, yet here is something that may have to be separated, although with difficulty, from the more narrowly speaking physiologic, as, for instance, the good effects of belladonna on the vascular spasms in the withdrawal symptoms of morphine. Specific psychoanalytic study of the effects of belladonna, however, may show that it is only another type of elatant, just as one knows that religious ecstasy "works." Here the entry into another ecologic horizon—psychotic it may be from one point of view—is of profound psychologic significance when the whole functional activities of the religious phenomena are given rigid valuation. It may be safely predicated that mankind en masse is not yet ready to let go of magic. Man is still theothymic, and in the ecstasy caused by drugs and in its accompanying mystic delirium man has from the earliest times identified himself with God.

DR. PAUL SCHILDER: In the psychopathic department of Bellevue Hospital, Dr. Bromberg and I have studied a large number of patients with alcoholic hallucinosis from an analytic point of view. In the majority of cases the patients fear castration and dismembering. One does not need the psychoanalytic technic to find that out. The material comes out in the voices which the patients hear. They are threatened with genital castration. Often the patient is also afraid that he will be cut into pieces, and, finally, there is in the foreground of the whole picture the fear of being dismembered completely. I have called this the dismembering motive. The unity of the body—the narcissism—is threatened. The patients fear not only that they may be castrated but that they may become objects of homosexual attacks. At the same time they are blamed and criticized by the voices. The voices tell them how bad they are, that they are sinners, and, especially, that they are degenerates and perverts. I emphasize these experiences because they show clearly that there is some change going on in the narcissistic sphere of the patient. He feels frightened and is afraid of losing the unity of the body—of being dismembered. It is the fear of punishment. The voices represent the conscience. It is a problem in narcissism, in the super-ego and in the ego-system. The homosexual fears are closely connected with a deep-seated fear of the loss of complete sexuality. I do not think that what one sees in alcoholic hallucinosis is true only for the alcoholic hallucinosis as such. One has the general experience that whatever is going on in a toxic psychosis has been a problem of the prepsychotic personality. Therefore I am glad that Dr. Radó emphasizes the problems of the ego, the narcissistic problems and the problems of the conscience in the drug addict and in the person with alcoholism especially. I think that these are much more important problems than the oral problem, which is also present in these cases.

One can say that what one sees in alcoholic hallucinosis is not only a psychologic problem; it is also a physiologic one. There is something going on in the

somatic sphere. Dr. Henry is right when he says that dogs can become drug addicts. I have seen proof of this in dogs that Dr. Hartmann has intoxicated with cocaine. Dr. Henry asked whether such dogs have feelings of guilt. Of course the dogs did not talk with me, but they also did not talk with Dr. Henry. So it is at any rate possible that something is going on that neither of us knows. I should like to add that the relation of the dog to the person who administers the drug is certainly important. At least the attitude of the dogs shows an enormous amount of transference, or, if one wishes, some sexual interest in the person who administers the drug. I should not have brought up this point if I had not wanted to emphasize that one has no right to say that this is psychologic and that that is toxic. Every psychic experience always has these two sides. The taking of a drug involves a psychic experience as well as a change in the body. I do not think that in the alcoholic intoxications there is only a "psychic" narcissistic phenomenon or an inflation of the ego. It is a matter of course that there is also a physiologic problem—a change in the brain and in the entire organism. I think, therefore, that one has no right to say that the psychologic begins at a certain place and the physiologic ends at a certain place; psychology and physiology are always present in these problems.

I wish to pass to the more important problem that practically all drugs which lead to addiction act in some way on consciousness. This is a rough formulation, but I make it in order to point to the fact that at least something is now known about the centers of consciousness. They lie around the third ventricle. Something is known about the sleep center; it is known also from histopathologic examinations of the brains of alcoholic addicts that something is going on in this region. That is not only true of the severe cases, let me say, of poliioencephalitis (encephalopathia alcoholica) on which I have worked with Dr. Bender. We found pathologic changes in this region. It is certainly also true of the alcoholic intoxications. In alcoholic intoxications vestibular phenomena and diplopia are present. Therefore, these problems have always two sides, and it is merely a methodologic question which side one considers in a scientific investigation. One is justified in omitting for a while the somatic side, because when these different investigations are carried on a long way they will doubtless meet. The same point of view is of course to be used in the problem of the personality of the drug addict. There must be something special also in his psychophysiologic constitution and in his relation to consciousness, to the ego and to the conscience. My rather incomplete experiences in this respect point indeed to the idea that the structure of these functions is already changed in the person who later will become a drug addict. I have the opinion that in persons who have a general weakness of this apparatus, it is certainly not only a weakness of the physiologic but also of the psychologic apparatus. It is a psychophysiologic point of view. These persons experiment and are continually trying out ways of changing this particular system, a system which is different from the system of other persons. They will experiment with drugs and with all the experiences of every-day life, and they will find their particular drug. The very choice of the drug is important. There are definite hints that in the personality of the cocaineist is much more homosexuality than in the personality of the person who later will become an alcoholic. It is true that the cocaineist, on the other hand, by means of the drug increases to an enormous degree the homosexual tendencies which were already strongly present, for every drug addict tries to find, and finally does find, the drug which fits his special pathologic needs. I think, therefore, that what follows from a drug addiction is the result of an experimentation which the drug addict makes with himself. In this experimentation, he uses drugs when he is unable to change his personality in an autoplasmic way. He uses the alloplasmic method in order to fulfil his deepest tendencies and desires. In such a conception it is evident that psychologic problems are closely interwoven with physiologic ones, or it would be even better to say that they are not interwoven—they are the same problem.

## PHILADELPHIA NEUROLOGICAL SOCIETY

*Regular Meeting, March 24, 1933*A. C. BUCKLEY, M.D., *President, in the Chair*

FACIAL HEMIATROPHY. DR. PAUL SLOANE (by invitation).

A girl, aged 10, who was admitted to the service of Dr. N. W. Winkelman at Temple University Hospital, had been perfectly well until four years ago, when she sustained an injury of the head in an automobile accident. She was unconscious for half an hour afterward and had a bruise on the left side of the neck below the ear. She complained of severe pain below the left ear. Three weeks later a lump developed at the site of the bruise. It was hard and inflamed; a physician made a diagnosis of mumps. One morning she suddenly began to vomit a matter similar to pus and blood, and following this the lump disappeared. For a year afterward, however, she complained of tenderness below and behind the ear. Four months after the accident the patient's mother noticed dryness and discoloration at the left angle of the mouth. Shortly thereafter the chin began to shrivel. In about five or six months the left cheek turned blue and the outer canthus of the eye began to draw in. About one year after the onset a line appeared which extended from the eye to the angle of the mouth, with similar wasting. The condition was treated with massage, irradiation therapy and medication. Tonsillectomy was also performed, but all measures were without effect. One year ago the child complained of numbness in the left cheek, which disappeared after six months. There is no hereditary history of a similar condition. The family history is negative for tuberculosis.

The two sides of the face appear to belong to different people. The right side is full and of normal contour, and looks like the face of a normal child aged 10; the left side is shrunken and looks like that of an old woman. The wasting begins at the midline of the chin and involves the chin, the lateral portion of the cheek, the malar region, the temple and the mastoid region. Over the atrophied areas the skin is bluish. The left side of the face is more moist to the touch than the right. The measurement from the midline of the chin to the angle of the jaw is 10 cm. on the right side and 9 cm. on the left. The measurement from the bridge of the nose to the external auditory meatus is 13.5 cm. on the right side and 11 cm. on the left side. The wasting does not involve the medial portion of the face. Roentgen examination of the bones of the face showed no difference on the two sides. The hair of the left eyebrow is sparse, particularly in the lateral portion. The skin is not adherent to the subcutaneous tissues but seems to be denser in certain areas. There is neither hemiatrophy of the body nor dermatographia. The basal metabolic rate is normal.

Various theories of the pathogenesis were discussed, the main emphasis being placed on those of the implication of the trigeminal and sympathetic nerves. In the case presented, there was at one time a numbness of the cheek which persisted for six months and then disappeared. The atrophy seems to follow the lamellar type of trigeminal lesions; its distribution corresponds to that of the nuclear sensory nerve as contrasted with that of the peripheral sensory nerve. Although these facts might indicate an implication of the fifth nerve, the atrophy extends beyond the confines of the trigeminus into the region of the cervical innervation (behind the mastoid and along the neck). On the other hand, there is evidence of involvement of the sympathetic nerves in the sparseness of the hair of the eyebrow and the pigmentary changes in the skin. There is no Horner's syndrome.

Any theory relating to involvement of the sympathetic nerve must account for cases in which section of the cervical sympathetic nerve has occurred (with Horner's syndrome) as well as for the case now under consideration, in which there is no such pathologic condition. Apparently there is some factor common to both types of cases. Clean section of the nerve practically never produces the

condition. Moebius' suggestion that infection is a common cause may be significant. In the case presented there were the factors of trauma and infection. Perhaps the common factor is an irritation of the sympathetic fibers. Such irritation may produce a chronic spastic condition of the vessels, with subsequent trophic changes. It was with this point in mind that sympathectomy was suggested in this case. As preliminary treatment to sympathectomy, fever therapy was tried, in view of the known vasodilator effects. It was thought that even temporary vasodilatation might produce sufficiently encouraging results to induce us to proceed with the operation. The patient has had eight injections of typhoid vaccine, but has shown no effects after one month.

## DISCUSSION

DR. WILLIAMS B. CADWALADER: A few years ago Dr. Langdon presented before this Society two patients in whom Horner's syndrome was present, with a moderate degree of atrophy of one side of the face. In each case there was enlargement of the thyroid gland. It was believed that the thyroid gland had pressed on the trunk of the cervical sympathetic nerve and in this way had been responsible for the development of Horner's syndrome and hemiatrophy of the face. It is interesting to recall that Kuré (*Die vierfache Muskelinnervation einschliesslich der Pathogenese und Therapie der progressiven Muskeldystrophie*, Berlin, Urban & Schwarzenberg, 1931) claimed to be able to produce atrophy of the muscles with resulting dystrophic changes by section of the sympathetic nerve supply. I do not believe that section of the trunk of the sympathetic nerve will be of benefit to this patient.

DR. N. W. WINKELMAN: This case has given rise to much discussion: First, as to the etiologic factor, the etiology is still a matter of speculation. In many cases that have been reported in the literature histories of antecedent infections and local traumas have been so common that they cannot be overlooked. An actual causative rôle has been postulated. Second, as to the nature of the condition. I believe we are coming around to the point of view that the sympathetic fibers are at fault in conditions of this nature. It is possible that the trophic changes are marked in lesions of the sympathetic nerves just as in irritative lesions of the peripheral nerves. For this reason section of the sympathetic fibers might be of value in arresting this process.

DR. B. J. ALPERS: This girl was for some time a patient in Dr. Weisenburg's clinic at the Philadelphia Orthopedic Hospital and Infirmary for Nervous Diseases. What interested us was the relation of the trauma to the facial condition. We surmised that the only connection between the two was the proximity in time. Another point of interest was that, although the child had been frequently examined, she was extremely well adjusted and was not self-conscious.

SUPERIOR PULMONARY SULCUS TUMOR. DR. SAMUEL J. SPERLING and DR. JOSEPH C. YASKIN.

We are presenting this patient before the Society because of the characteristic neurologic syndrome which this uncommon lesion produces.

J. L., a Jewish man, aged 62, was admitted to the Philadelphia General Hospital in the service of Dr. Robertson on March 10, 1933, and was subsequently transferred to the neurologic service of Dr. Yaskin. He complained of pain, which began in his right wrist in May, 1932, and later spread to the ulnar aspect of the hand, forearm, arm and axilla. The pain was excruciating and burning. At first it was intermittent, lasting several hours, but since November it has been constant and prevents the patient from sleeping. The pain is uninfluenced by coughing, sneezing or straining and is occasionally relieved somewhat by heat. There are associated paresthesias of "pins and needles" or of "running cold water" in the right arm. In July the patient noted weakness of the right hand, which has progressed so that he has lost all power of intrinsic motility of the fingers. He also observed weakness of some movements of the forearm and arm. About eight

months ago he noted slight blurring of vision and drooping of the right upper eyelid. Other symptoms are slight dyspnea on exertion, nocturia once or twice each night, and a loss of 10 pounds (4.5 Kg.) since May, 1932.

Physical examination disclosed poor heart sounds, a blood pressure of 140 systolic and 60 diastolic, occasional wheezing râles in an emphysematous type of chest, questionable diminished breath sounds and a percussion note at the apex of the right lung, a moderately enlarged lymph node in the right axilla, a palpable liver and a slightly enlarged prostate.

The significant findings on neurologic examination were: marked Horner syndrome on the right, with enophthalmos, miosis and ptosis of the eyelid, but no disturbed sweating; atrophy of the muscles of the right hand and forearm, chiefly on the ulnar aspect; atrophy of the triceps, and, probably, slight atrophy of the biceps and of the coracobrachialis and the pectoral muscles. There was no motility of the fingers in any direction. The extensor power at the wrist was slight, and there was marked weakness of extension, pronation and supination of the forearm and of adduction of the upper arm. Flexion of the forearm, abduction and rotation of the upper arm and elevation of the shoulder were performed fairly well. The neck and head seemed slightly inclined to the right, and there was a slight elevation of the right shoulder, which was associated with spasm of the trapezius muscle. No radial, triceps, Hoffmann or pectoral reflex was obtained on the right, while the biceps reflex was diminished. All forms of sensation (touch, pain, heat, cold, position and vibration) were impaired in the areas supplied by nerves from the seventh and eighth cervical and the first and second dorsal dermatomes extending to the apex of the axilla. The right hand was somewhat edematous, and the skin was shiny. Occasional fibrillations were noted in the upper arm.

Laboratory studies showed normal urine and a negative Kahn test of the blood. The blood sugar was 91 mg., and the urea was 15 mg. The spinal fluid was clear; there was a trace of albumin but no cells. The Wassermann reaction was negative; the colloidal gold curve was 0012210000.

Roentgen examination, made by Dr. Ostrum, showed a normal heart and normal lungs, except for increased density at the apex of the right lung, with rarefaction of the second and third ribs posteriorly. There was questionable rarefaction of the lamina of the seventh cervical vertebra on the right. The diagnosis was superior pulmonary sulcus tumor.

*Comment.*—In his presidential address before the Section on Radiology at the eighty-third annual session of the American Medical Association Dr. Pancoast (Superior Pulmonary Sulcus Tumor, *J. A. M. A.* 99:1391 [Oct. 22] 1932) reported seven cases of what he called superior pulmonary sulcus tumor. These tumors have a characteristic neurologic and radiologic syndrome. "The tumors in question seemed to occur at a definite location at the thoracic inlet, were characterized clinically by pain around the shoulder and down the arm, Horner's syndrome and atrophy of the muscles of the hand and presented roentgenographic evidences of a small, homogeneous shadow at the extreme apex, always more or less local rib destruction and often vertebral infiltration." The neurologic symptoms are due to involvement of the lower cervical and upper thoracic nerves just lateral to the vertebral column and therefore affect the oculosympathetic fibers. The pathologic nature and origin of the tumor are as yet undetermined.

#### DISCUSSION

DR. J. W. McCONNELL: About a year ago I presented before the conference of the neuropsychiatric staff of the Philadelphia General Hospital a man with symptoms similar to those shown by this patient. He had a definitely palpable tumor in the supraclavicular region, with enlargement of the glands of the neck on the side affected, and the neurologic features of the Dejerine-Klumpke syndrome. Unfortunately, an acute hemiplegic attack developed, which involved the side affected by the sulcus tumor, and the patient died before the examination could be completed. The diagnosis was made clinically, and the roentgen findings were interpreted by

both our laboratory and by Dr. Pancoast as confirmatory of the symptomatic diagnosis. Unfortunately, we were unable to secure a necropsy.

DR. WILLIAM G. SPILLER: The first patient mentioned in the paper by Dr. Pancoast was formerly under my care. Dr. Pancoast obtained a roentgenogram showing a shadow suggesting a tumor at the apex of the lung, and this permitted a correct diagnosis. Another patient mentioned in his paper has also been under my care. The clinical findings are usually those of Klumpke's paralysis, with involvement of the roots of the lower cervical and upper thoracic nerves and of the ocular sympathetic fibers leaving the cord at the roots of the eighth cervical and first thoracic nerves.

PROGRESSIVE BULBAR PARALYSIS WITH A HISTORY OF FAMILIAL OCCURRENCE.  
DR. MELBOURNE J. COOPER.

Progressive bulbar paralysis, or glossolabiolaryngeal paralysis of Duchenne (Duchenne, G. B. A.: *Paralysie musculaire progressive de la langue du voile du palais et des lèvres*, *Arch. gén. de méd., Paris* **16**:283 [Sept.] 1860) is ordinarily considered a degenerative disease of the declining years of life, affecting primarily the motor nuclei of the twelfth, seventh, tenth, ninth, eleventh and sometimes the fifth cranial nerves approximately in that order of frequency, and, to a lesser extent, the pyramidal tracts in the brain stem. It is of infrequent occurrence and is characterized clinically by dysarthria in the early stage, followed by paralysis and atrophy of the tongue, progressive weakness of the lower part of the face, dysphagia, palatal weakness and weakness of the laryngeal muscles. The disease usually runs a course of from one to four years, inanition, aspiration pneumonia or respiratory paralysis terminating the picture.

The etiology is unknown. Dana (Textbook of Nervous Diseases, ed. 10, New York, William Wood & Company, 1925, p. 311) mentioned that 20 per cent of the patients have had syphilis, but this has not been a prominent factor in the experience of most investigators. It is generally recognized that a form of bulbar paralysis may occur, usually as the terminal condition, but sometimes in the earlier stages of amyotrophic lateral sclerosis, progressive spinal muscular atrophy, syringobulbia, progressive ophthalmoplegia (superior poliomyelitis) and tabes dorsalis. However, true progressive bulbar paralysis of the Duchenne type is considered a separate entity. Spiller (cited by Osler, William, and McCrae, Thomas: *Modern Medicine*, ed. 3, Philadelphia, Lea & Febiger, 1928, vol. 6, p. 115) stated that "The bulbar paralysis of Duchenne is a pyramidal amyotrophic sclerosis descending in type," and mentioned that for a long time there had been no satisfactory case in which necropsy showed intact pyramidal tracts. Probably only one case, that of Guillaumin, Alajouanine and Bertrand, reviewed by Spiller (*Diseases of the Nervous System, Progressive Med.* **3**:251 [Sept.] 1926), has shown the pure form of bulbar paralysis without implication of the pyramidal tracts. Spiller believed that the disease is probably an abiotrophy. Lovell (*Familial Progressive Bulbar Paralysis*, *ARCH. NEUROL. & PSYCHIAT.* **28**:394 [Aug.] 1932), reported a case of progressive bulbar palsy in a woman, aged 66, whose mother, maternal uncle and maternal uncle's one son had succumbed to probable bulbar paralysis which had developed in the sixth or seventh decades of life. I have found no other record of presumably direct heredity of the Duchenne type of progressive bulbar paralysis in the available literature, though Bernhardt (*Beitrag zur Lehre von den familiären Erkrankungen des Centralnervensystems*, *Virchows Arch. f. path. Anat.* **126**:59, 1891) mentioned the familial occurrence of similar degenerative diseases, bulbar paralysis having developed secondarily in several cases cited by him.

The patient I am presenting gives a history of the occurrence of a condition which probably represents the Duchenne type of the disease in members of three generations of her family.

M. S., a woman, aged 52, was studied in the service of Dr. William G. Spiller at the Hospital of the University of Pennsylvania in February, 1933. She was apparently in good health until August, 1932, when her daughter, with whom she

lived, noticed a slight indistinctness of the patient's speech; her words seemed to run together as she talked. There were no other symptoms at that time. In November, the patient began to experience some difficulty in swallowing, and occasionally would strangle. These symptoms progressed slowly but steadily, and by the time of the patient's first visit to the hospital there were a decided indistinctness of speech and a considerable difficulty in swallowing. There had never been any evidence of palatal weakness, and she had noticed no weakness or spasticity of the limbs. Throughout her life the patient had suffered from migrainous attacks characterized by severe frontal headaches, with vomiting and lacrimation; these attacks occurred perhaps once every two or three weeks. She had inflammatory rheumatism for one month at the age of 30. The medical history was otherwise nonessential.

The following family history was obtained from the patient and her daughter, both of whom are intelligent women and are ostensibly reliable in their statements. The mother of the patient died between the age of 60 and 70, within one and one-half years after the onset of the same symptoms that the patient now shows, i. e., a disturbance of speech and of deglutition. In addition, however, within one year after the onset paralysis of the lower limbs developed, which was thought to be of the flaccid rather than the spastic type. The upper limbs remained unaffected throughout the illness. Before death there was complete paralysis of the swallowing function.

The mother's sister showed the same bulbar symptoms between 50 and 60 years of age and died within about two years after the onset. Whether or not the limbs were affected is unknown. The mother's brother had similar symptoms, which first appeared at the age of 42 or 43. He died within fourteen months after the onset, having become unable to swallow before death. His limbs were not affected. The maternal grandmother of the patient had the same syndrome which began at the age of 70. She died within one and one-half years after the onset, the limbs being unaffected. The brother of the maternal grandmother showed the same symptoms when he was "along in years" (the exact age is unknown). It is not known whether or not his limbs were affected. None of these relatives received treatment in a hospital, and more precise accounts of their symptoms are not available at the present time. An effort is being made to obtain further data, but it has been unsuccessful thus far.

The other members of the patient's family are the father, who is living and well at the age of 78, and ten children of her own, who are all living and well. One brother was stillborn; a sister died at the age of 10 of appendicitis; the twin sister of the patient died at the age of 6 months of "summer complaint."

Examination revealed moderate arteriosclerosis which was not disproportionate to the age of the patient. The blood pressure was 120 systolic and 72 diastolic. Neurologic examination showed a distinctly thick and slurring speech, the characteristics being a tendency to run words and syllables together and to show very imperfect enunciation, particularly of the tongue consonants (e, g, r, l), the stopped lip consonants (e, g, p, b) and the stopped tongue and teeth consonants (e, g, t, d). There was limited voluntary movement of the tongue. It could be protruded only a little beyond the incisor teeth and could be pressed against the inner surface of either cheek with much reduced power. The muscles on both sides of the tongue were atrophic and showed marked fibrillation. All these signs were more pronounced on the left. Percussion of the tongue produced distinct myo-edema. All voluntary movements of the palate appeared normal, and the palatal reflex was preserved. The vocal chords were freely movable and approximated well voluntarily. The muscles of the lower part of the face on each side appeared to be weak in voluntary movements, but they were not paralyzed. There was possibly a slight weakness of the orbicularis palpebrarum on each side, but this was uncertain. There may have been a slight impairment of convergence of the eyeballs, but this too was indistinct and was not constant.

There was moderate exaggeration of all the tendon reflexes, which was equal on the two sides. The epigastric and lower abdominal reflexes were not obtained,

possibly because of the relaxed state of the abdominal muscles. There was no Trommer sign. The Babinski sign was positive on the left and suggestive but inconstant on the right. The Gordon and Oppenheim reflexes were positive on each side; the Rossolimo sign was negative; there was neither ankle nor patellar clonus. Motor power and coordination of all limbs seemed to be entirely normal. All forms of sensation were normal throughout. Careful scrutiny of the condition of the upper and lower limbs, including the muscles of the shoulder girdle, the intrinsic muscles of the hands and the peroneal muscles, failed to reveal any distinct atrophy, focal weakness or fibrillation. The Wassermann test of the blood gave negative results.

*Comment.*—The case is regarded as one of the Duchenne type of progressive bulbar paralysis. Cognizance is taken of the fact that the disease is in all probability pyramidal amyotrophic sclerosis, as was stated by Spiller, and that as such it might be considered as closely related to the more frequent form of amyotrophic sclerosis which affects the cord below the medulla in the early stages and ascends later to the medulla. The occurrence of diseases of the cord with bulbar symptoms in several members of the same family has been noted several times (by Bernhardt and by Dejerine, J.: *Sémiologie des affections du système nerveux*, ed. 2, Paris, Masson & Cie, 1926, p. 156). Such a strongly suggestive family history as that accompanying this case has not been reported so far as I am aware, except by Lovell in his description of a case of probably true progressive bulbar paralysis.

It is not possible to determine conclusively the true nature of the disease that affected the other members of the patient's family, but the evidence in favor of a familial occurrence of the Duchenne type of progressive bulbar paralysis appears to be strong. According to the informants, who have given the same information regarding the family history at several different times, the conspicuous and early manifestations of the disease in each affected member were disturbances of speech and of deglutition. It is reasonable to assume that these signs would be easily recognized by a layman. However, it cannot be determined absolutely that the patient's mother had a flaccid type of paralysis of the lower limbs with complete noninvolvement of the upper limbs, as the statement of a competent judge regarding the type and degree of paralysis in that instance is lacking. It is hazardous, therefore, to attempt to rule out a spastic paresis more distinct in the lower limbs and due to involvement of the pyramidal tracts in the brain stem. In no other member of the family was there paraplegia, so far as the informants know; it is definitely stated that there was bulbar paralysis without involvement of the limbs in two of the affected members. In view of this information, which seems as reliable as might be expected from persons other than trained medical observers, it is thought that in all probability true progressive bulbar paralysis affected the maternal grand-uncle, the maternal grandmother and four of the direct descendants of the latter, including the patient.

#### DISCUSSION

DR. WILLIAMS B. CADWALADER: I examined the patient while she was in the hospital. It is extraordinary that progressive bulbar palsy should develop in many members of the same family, and except for the report to which Dr. Cooper has alluded I do not remember hearing of this fact before. The cause of progressive bulbar palsy is unknown. It is usually believed, however, that it belongs to the general group of diseases called by Gowers abiotrophy. This theory has never seemed correct to me. I recall a case reported before this Society by Bailey (Involvement of Nervous System Following Extraction of Teeth, *J. Nerv. & Ment. Dis.* **73**:180, 1931) in which the symptoms of progressive bulbar palsy developed soon after the extraction of infected teeth, thus suggesting a possible relationship to some toxic or infectious process.

In discussing the filtrable viruses and their modes of entry into the central nervous system in relation to certain diseases, particularly epidemic encephalitis and poliomyelitis, Rivers (Relation of Filtrable Viruses to Disease of the Nervous System, *ARCH. NEUROL. & PSYCHIAT.* **28**:757 [Oct.] 1932) said: "The most

obvious possible portals of entry of viruses into the central nervous system are: (1) by way of the blood stream; (2) by means of the perineural spaces; (3) by direct extension along nerves, accomplished by the propagation of the active agents through the cells of the neurilemma, and (4) by way of axis-cylinders of nerves within which the incitants grow until the bodies of the cells themselves are reached." From these facts, some of which are yet unproved, I am inclined to believe that some cases of progressive bulbar palsy may perhaps be dependent on the transmission of a virus through an axis-cylinder or through a nerve trunk, the infection eventually reaching the nuclear cells of the cranial nerves. If this is so, the theory of abiotrophy must be modified or discarded. I would emphasize, however, that there is no evidence to warrant the assumption that progressive bulbar palsy is the manifestation of any form of infection in which the causative agent has been demonstrated.

DR. WILLIAM G. SPILLER: Progressive bulbar palsy in adults has not been considered a family form of disease, and it is necessary to be cautious in accepting evidence in cases of this kind, especially when the facts are given only by members of the family who are not trained observers and whose statements depend largely on hearsay. Dr. Cooper has presented the best description of symptoms obtainable, and the case he presents may be regarded as suggestive of a family disorder. Patients may not distinguish pseudobulbar palsy or parkinsonism in asserting that the same condition as the bulbar palsy with which they are affected has occurred in deceased relatives.

Whether progressive bulbar palsy ever occurs without involvement of the pyramidal tract has long been a matter of doubt; it was not recognized by Leyden or Dejerine. I have watched in vain during many years for such a case with necropsy. What seems to be a reliable case was reported by Guillain, Alajouanine and Bertrand (*Rev. neurol.* 1:577, 1925).

ENCEPHALOMYELITIS FOLLOWING THE USE OF SERUM AND VACCINE: A REPORT OF TWO CASES, ONE WITH AUTOPSY. DR. N. W. WINKELMAN and DR. NICHOLAS GOTTEN.

We report two cases of encephalomyelitis, one in which the disorder followed the use of serum other than that for rabies, the other in which the condition developed after the use of vaccine for the prevention of variola. The first patient in whose case there are autopsy observations, received horse serum for the control of bleeding after the extraction of a tooth. An infection of the upper respiratory tract developed shortly afterward. The condition in the second case is a complication following the use of a combined vaccine of streptococcus and colon bacillus for the treatment of psoriasis. In the first patient serum sickness developed after the injection. Three weeks later she contracted an infection of the upper respiratory tract, following which symptoms of encephalomyelitis became prominent. She died of this condition seventy-two days after the onset. Pathologically, the brain and cord contained areas of inflammation and necrosis; the meninges showed an inflammatory reaction. These areas differed from the areas found in multiple sclerosis in that differential staining showed cells of a chronic inflammatory type. The second case was that of a white woman, aged 28, in whom symptoms of encephalomyelitis developed following the third injection of vaccine. One week later a fourth injection of vaccine caused rather severe symptoms of encephalomyelitis. The condition gradually improved, and the patient made an almost complete recovery.

Experimental work shows that most cases of encephalomyelitis have developed as a result of a combination of agents, usually a vaccine or virus with an activating agent such as an infection. In our first case there is a history of an injection of serum and the development of symptoms following the contraction of acute coryza. In our second case the onset of the neurologic symptoms followed within a few hours the third and fourth injections of vaccine.

## DISCUSSION

DR. WILLIAM G. SPILLER: This paper is of special interest because of the unusual etiology: horse serum in the one case and vaccine made from streptococci and colon bacilli in the other. The type of postvaccinal encephalitis which has aroused the most attention is that following vaccination against variola, especially in Holland. An abstract by Alpers of a paper by Bastiaanse on this subject appeared in the March, 1933, issue of the ARCHIVES, page 638. The most acceptable explanation for the phenomenon is that the vaccine activates a latent virus. This view is supported especially by the fact that the vaccine which has not produced encephalitis in this country has done so when employed in Holland. The paper by Gotten and Winkelman resembles the paper on encephalomyelitis disseminata written by me (Encephalomyelitis Disseminata, ARCH. NEUROL. & PSYCHIAT. 22:647 [Oct.] 1929), in that in each paper two cases are described, of which one resulted in recovery and the other came to necropsy; the observations at necropsy were similar.

Encephalomyelitis disseminata was known before Redlich called attention to it, but he aroused a latent interest in the disorder, although he had but one necropsy and that was unsatisfactory. In a case of subacute multiple sclerosis studied and reported by me (The Subacute Form of Multiple Sclerosis, ARCH. NEUROL. & PSYCHIAT. 1:219 [Feb.] 1919), the course was of about two years' duration. Rabbits are hardly suitable for experimental work on encephalitis, as findings suggesting encephalitis have been obtained in apparently healthy rabbits. Globus believes that an infectious agent must be postulated for a diagnosis of encephalomyelitis, but it may be difficult to determine such an agent, especially in acute multiple sclerosis.

It is strange that serum causes encephalomyelitis in some instances and brachial plexus neuritis in others. I studied three cases of the latter type, in two of which the condition was produced by antidiphtheritic serum; in the third case it was caused by tetanus antitoxin. These cases were cited in a paper by Wilson and Hadden with three cases of their own (Neuritis and Multiple Neuritis Following Serum Therapy, ARCH. NEUROL. & PSYCHIAT. 26:1353 [Dec.] 1931).

## Book Reviews

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**Zur Klinik und Analyse der psychomotorischen Störung.** By Otto Kauders. Sonderausgabe von Heft 64 der „Abhandlungen aus der Neurologie, Psychiatrie, Psychologie und ihren Grenzgebieten.“ Price, 12.60 marks. Pp. 132. Berlin: S. Karger, 1931.

In addition to his original contribution to the problem of motility disorders in psychotic patients, Otto Kauders presents in this monograph a comprehensive review of the work of investigators responsible for the actual state of knowledge in this domain. The reader will find in this volume a thorough follow-up, in a necessarily condensed form, of the development of neuropsychiatric thought in regard to this problem. Wernicke, who coined the expression “psychomotor disturbances of the psychic arc-reflex,” and Kleist, his closest follower as well as original investigator, represent the neurologic concept of psychomotility. In Wernicke's psychic arc-reflex, the latter does not differ fundamentally from any other primitive reflex, its passage through the psychic sphere being only an epiphenomenon. Kleist has enlarged greatly, on a descriptive level, Wernicke's work in studying the extreme polymorphism of hyperkinetic movements, in systematizing the concept of motility psychosis and in establishing the presence of typical motility reactions in certain syndromes. Kleist follows Wernicke in placing in the forefront the neurologic aspect: He primarily discusses the connection of motility disorders with organic diseases of the cerebrospinal nervous system, i. e., with the nature and localization of pathologic processes. Experience with epidemic encephalitis is in large part responsible for localizing the anatomic substratum of psychomotor disorders chiefly in the basal ganglia—particularly in the striate bodies. Kleist's theory, being predominantly of neurologic character, emphasizes nevertheless the dependence of psychomotor reactions on psychic phenomena without, however, attempting thoroughly to investigate the nature of such dependence.

Another concept, propounded by Kraepelin and other investigators, may be qualified as a psychologic one. Taking for granted that abnormal motor reactions express mental reactions, the advocates of this concept are not, however, sufficiently concerned with the nature and content of the essential elements in the relationship between these two phenomena. Most of the hyperkinetic and akinetic conditions in psychotic patients would primarily be the result of disturbances in the sphere of volition. By that Kraepelin and his school understand that such disturbances take place not as a result of conscious will and intention, but rather as a reaction to impulses responsible for the voluntary act, the impulses being caused by affective disorders.

Bleuler and his followers, particularly Klasi, offer a theory which bears evidence of the influence of the psychoanalytic school and has been adhered to by psychoanalytic authors. In harmony with the psychoanalytic interpretation of neurotic symptoms, the origin of psychomotor disorders is directly related not only to conscious but also to unconscious psychic phenomena, most of which are of complicated nature. On the other hand, Bleuler speaks of automatic movements which he interprets as such in most motility disorders in patients with schizophrenia.

The object of Kauders' investigations was to study the attitude and behavior of the psychotic patient toward the abnormal movements of his body, be the movements of organic or psychogenic origin, and, conversely, the effect which the perception of the abnormal motility might have on both the pathologic mental processes and the motor reactions themselves. For that purpose, Kauders used psychotic patients in the acute phase of their illness. Spontaneous utterances of the patient constituted the main material; less significance was attributed to catam-

nostic data obtained after the acute phase of the disease had declined. The intimate interrelationship between motor and mental reactions in psychotic patients with choreiform encephalitis, that is, in cases with neurogenic motor disturbances, is discussed in the light of the recorded case histories. These suggest that, notwithstanding the fact that the motor disturbances are considered to be of organic origin, these disturbances cannot be looked on as merely bodily symptoms, foreign to the whole personality; the clinical data at hand show rather that mental and especially affective elements contribute to the occurrence and shaping of the abnormal movements, that the latter are used by the patient to express personality reactions. The intimate connection between mental reactions accompanied by high affective tension and motor restlessness finds illustration in the following so-called reproduction experiment: The patient, in whom the motor disorders have markedly decreased, is asked to repeat voluntarily some of his previous pathologic movements. In reproducing more or less adequately the experienced jactations and tremors, the patient rapidly becomes the victim of motor disorders which have all the characteristics of his former disorders, of which he has a hard time to rid himself. At the same time, one observes the clinical mental picture which in the acute phase of psychosis paralleled the motor reactions. It is noteworthy that not only did such reproduction experiments prove successful in essentially psychotic patients, in whom one might assume that it is relatively easy, even in periods of distinct improvement, to elicit their dominant psychic experiences; the experiments also succeeded fully in cases of epidemic encephalitis with psychosis, in which the clonic-choreiform movements were subject to the influence of psychomotor restlessness. In these patients also, while they were in phases of relative motor rest, the motor disorders of the acute period of the illness were induced and at the same time the correlated mental reactions, in most cases in a mild form, came to the fore. The most conspicuous feature in these artificially elicited personality reactions was the affective state, which displayed as high a tension as that of the climax of psychosis and motor restlessness. The principle of the reproduction experiment was also applied to patients with delirium tremens. When these patients were in the immediate postdelirium period, the hypnotic suggestion of certain motor reactions of the delirium phase not only was followed by further development of the original motor restlessness, but also brought forward a delirious state, which, being in many respects quite different from the actual delirium tremens, on the whole stood very close to it. Here, again, as in the experimental studies in acute psychoses with hyperkinesia, Kauders demonstrates the interdependence between the motor and mental reactions and their parallel course. A comparative study of the observations made in experimenting with these two different types of mental reactions shows, however, quite marked differences: In the previously described reproduction experiments—when they are successfully carried out in acute psychosis—one usually provokes vivid and sustained motor reactions, which, in their essential characteristics as well as in details, are similar to the original spontaneous motor restlessness. On the contrary, the motor reactions induced by hypnosis in cases of delirium tremens represent only a "motor memory" of the original reactions and are of short duration. One does not succeed in eliciting the stereotyped occupational movements or movements of other nature, as described in the case history, but one obtains rather a condition of motor restlessness with tremors of the extremities which one commonly observes in alcoholic delirium. Furthermore, while the reproduction experiment in the acute psychosis brings to the fore illusion and hallucination complexes which dominate the hypnotic condition, the postdelirium hypnosis induces neither occupation delirium nor optic hallucinations of the type of delirium tremens. One sees developing rather a state of hallucinosis which commonly does not occur in acute delirium, but which is somewhat similar to those typical alcoholic delirious conditions in which "scene" hallucinations take the upper hand. Not unmindful of the disparities noted between the responses to suggestion of the acute psychotic patients on the one hand and the reactions of the patients with delirium tremens on the other, Kauders on the basis of his clinical and experimental data feels justified in asserting that, so far as his clinical material is concerned, both patients

with acute psychosis and those with delirium tremens showed evidences of the existence of intimate connection between motor and mental reactions. In neither of these psychotic reaction types could motor restlessness be elicited separately; in each of them motor disorders could be understood only as being elements of personality reactions, to the same extent as are verbal expressions. In this respect the author's study of a case of hysteria presents a particular interest: The patient was a woman suffering from typical attacks of hysteria on a sexual traumatic basis. At the moment when she started telling the painful story of her experienced sexual outrage, she abruptly stopped talking and immediately, without showing evidences of emotional upset of any significance, went through a hysterical motor attack. Here, to all intents and purposes, the motor reaction seems to act as a substitute for verbal expression, and, as such, seems to continue the story; what the patient could not or did not want to talk about was dramatically expressed in movements.

As to the attitude of the patient to his motor disorders, it appears to be a heterogenous one. The scrutiny of the patient's interpretations of his movements, as exemplified in the two cases of choreiform encephalitis, leads Kauders to distinguish the following attitudes: The one attitude, as observed in one psychotic encephalitic patient, is a rational one. The reasoning capacity of the patient, remaining untouched by the pathologic psychic condition, enables him to remain a critical observer of his motor reactions; he is cognizant of the fact that the latter are abnormal and signify disturbances in his organism. On the other hand, the recorded utterances of the other patient with encephalitis in regard to his motility make it clear that the motor disorders enter into his delirious content as a nondetachable component. From the standpoint of the delirious personality, the motor restlessness has a meaning and a definite goal: It is a voluntary personality reaction so far as it is a response to optic hallucinations, or a defense reaction against tactile, kinesthetic and other bodily sensations. Finally, some verbal expressions of the same patient suggest that the motor reactions are not altogether foreign to the sane personality; they seem to be somewhat in unison with the aims and mode of expression of the personality, but they are not always consciously envisaged in the sense of voluntary movements.

The instructive original material, being discussed in the light of bibliographic data, makes the monograph well worth reading.

**Einführung in die Psychoanalyse.** By Dr. Harald Schultz-Hencke. Price, 18 marks. Pp. 381. Jena: Gustav Fischer, 1927.

As an introduction, this work is unusually personal and by no means an expose of the stereotyped analysis. One deals here with an account by a special worker, enticing through a freshness of plan, but after all definitely difficult to grasp. It seems to presuppose much personal work or familiarity with the author's ways of thinking and range of experience. He begins interestingly with the "factual material," the sources of pleasure in childhood, the threats and hazards of these pleasure experiences, the normal effects of the threat and the types of miscarriage. Then follows a discussion of the therapy, its goal, the way and the technical detail, education in psychotherapy, the advising function of the analyst, the relation to hypnosis and the indications for analytic treatment. A discussion of fundamental principles then leads to the relations of psychoanalysis to philosophy, world views, public life, pedagogy, law and penology, and marriage.

Such a topic as pleasure in childhood is discussed more specifically than in most works: the oral domain and the weaning process; the "intentional domain" and conquest of the world and pictorial thinking; the epidermal domain, tenderness and masochism; the anal domain and training for cleanliness; the urethral domain; the manual domain, play, sadism and the prohibition of destruction; the genital domain, the world of fanciful wish, the latency period; the "gaps" in the sick and in the normal, and their frequency in the various domains, and the grouping of the causes. It is easy also to see the independence of the author and the naturalness and freshness of the point of view and interests in all the other topics or

chapters. But the discussion is not so simple as the groupings and the suggestive outline. In a field of such great individuality of the material and of the analyst, one needs an abundance of basic material. Instead of that, one meets with a decidedly taxing complexity of discussion. One doubts at times how far independence would be allowed to go unchallenged even in the author's own camp. The author assures one that Freud's very complete presentation of the structure of the theory should lead one not to expect novelty in the material. The mode of presentation is suggestive of an aim to go further, but the presentation is by no means always as lucid as one might expect of an introduction. One might hope for considerably more factual presentation or understructure for the frequently searching discussions, and therewith a fulfilment of the impression throughout that the author has a valuable contribution and expansion of psychoanalytic thought to offer.

**Die Allgemeinerscheinungen der Hirngeschwülste.** By Ferdinand Kehrer. Price, 10.50 marks. Pp. 116. Leipzig: Georg Thieme, 1931.

In this monograph the author gives a comprehensive review of the common symptoms of tumor of the brain (part I) with chapters on headaches, vertigo, papilledema, nystagmus, changes in the spinal fluid, psychic disturbances and other conditions. In this part one is especially appreciative of the description of the methods of Bailliant and of Baurmann for taking the retinal arterial pressure and the retinal venous pulse. These methods, while holding a limited usefulness in practice, indicate new approaches to a difficult problem: the relationship of the retinal circulation to the cerebral and systemic circulation. These methods have received scant attention in the American literature. The chapter on mental disorders with tumor of the brain stresses the euphoria and *Witzelsucht*. The presentation is complete but complicated and, as is usual with such presentations, fails to differentiate between delirious support disorders and organic defect disorders. This is an approach, however, which is not heeded by the German (and most of the American) psychiatric literature dealing with the mental aspects in somatic disease.

Part II deals with some less common findings: pain reflexes of the trigeminal and occipitalis regions, of the skull itself and of the extremities (Bikeles, Marie-Foix, Lasègue, Kernig). The sucking reflex, increase in the jaw jerk and change in the reactivity of the nasal mucous membranes to a graduated scale of irritants are mentioned as other methods of testing the trigeminal area. No mention is made of the brain stem reflexes of Guillain.

This monograph is usefully annotated with references to the original material and gains in authenticity from the author's personal experience. It furnishes a denial of E. Sach's statement of 1930 that "fifteen years ago, general discussions of tumors of the brain were usual. Today no such general discussion is of value." The neurosurgeon has revolutionized the approach to tumors of the brain so that exploratory procedures of one sort or another are every-day occurrences. There must remain, however, a large group of physicians who will always regret the exploratory operation as a diagnostic procedure, and to these this book will be most welcome.

**Anatomisch-histologische Untersuchungen über das sympathische Nervensystem.** By F. Kiss. Price, 10 marks. Pp. 252, with 189 figures. Szeged: Szeged Városi Nyomda és Könyvkiadó Rt., 1932.

The author stresses the importance of the size and myelination of nerve fibers as indexes of their functional significance and connections. One must be on guard, however, against relying too implicitly on such histologic characteristics and attempting to determine functional significance solely on this basis. The attempt to do so has led Professor Kiss into error. He states that all unmyelinated fibers are sympathetic; that there is no evidence that any sympathetic fibers are myelinated. His assumption that all somatic motor fibers are large leads him

to the conclusion that the small myelinated fibers in the ventral roots of the cervical nerves belong to the parasympathetic group. Although it is well known that the largest sensory fibers are those which supply the skeletal muscle, their histologic resemblance to somatic motor fibers causes him to question their sensory nature when he sees them in the dorsal root. The idea that all unmyelinated fibers are of sympathetic origin leads him to the conclusion that, since the vagus as it passes through the diaphragm is composed chiefly of unmyelinated fibers, it consists for the most part of fibers derived through anastomoses with the sympathetic system. The work of Professor Kiss furnishes an illustration of the danger involved in drawing general conclusions from incomplete data and then, when observations are made which will not fit in with these conclusions, giving to these contrary observations a false interpretation in order to avoid modifying the general thesis.

By prolonged staining with osmic acid after fixation in solution of formaldehyde, some cells in the spinal and sympathetic ganglia acquire a black color. Without any satisfactory reason the author concludes that these dark cells are postganglionic sympathetic neurons, and that the more lightly stained ones are sensory. On the basis of such evidence he further concludes that the spinal ganglia contain many sympathetic cells, and he ignores the good evidence to the contrary furnished by the silver stains.

**Anger in Young Children.** By Florence L. Goodenough, University of Minnesota Institute of Child Welfare. Monograph Series, no. 9. Price, \$2. Pp. 278. Minneapolis: University of Minnesota Press, 1932.

This book gives an observational study of the frequency, duration, causes and methods of handling outbursts of anger in young children in the home. Based as it is on daily reports made by a group of mothers, it may be questioned because of the possible prejudice or lack of objectivity. The reports on the children's behavior were not checked by a second observer. The author is well aware of this disadvantage and has attempted to make the reports as reliable as possible by care in the construction of the daily record sheets and by choosing mothers whose education was superior to the average. Unfortunately the group included only forty-five children, who ranged in age from 7 months to almost 8 years. Thus when divisions were made on the basis of age, sex and the like, the subgroups were extremely small. In view of the small numbers and the uncertain reliability of the records, the conclusions are largely tentative and require support from further studies. It seemed evident, however, that the outbursts of anger were most frequent during the second year; that after 2 years they were more frequent in boys than in girls; that the behavior during anger became more overtly directed toward a given end as age increased, and that the frequency of the outbursts was related both to imperfect health at the time of observation and to illness in the previous history.

The study as a whole is well presented, and the author's discussions of methods of control and parent-child relationships are particularly interesting. It is not her purpose to recommend promising methods for particular cases, but her comments on situations brought to light by the records offer many valuable suggestions with regard to the methods of handling outbursts of anger.

**Growth and Development of the Child: Part I. General Considerations.**

Report of the Committee on Growth and Development, White House Conference on Child Health and Protection. Kenneth D. Blackfan, M.D., Chairman. Price, \$3. Pp. 380. New York: Century Company, 1933.

The White House Conference on Child Health and Protection was very productive, not only in that it stimulated interest in this important subject, but also in that a series of volumes under the directorship of Kenneth D. Blackfan has appeared. These books were written by authors qualified to discuss the various aspects of

this problem, and the volumes have been so planned that they present in a logical manner all that is known on the subject.

The present volume is an introductory one in a series of four which supplement it. The contributors discuss chiefly the question of the growth and development of the child. Particular subjects under discussion are heredity and environment, fraternal and identical twins, the factors influencing differences in human types, sleep and repose, fatigue and so forth. It would be difficult to point out any particular aspect of this volume as most interesting, for all of it is worth reading, but perusal of the book shows that the sum total of knowledge of growth, particularly normal growth, is not very adequate, and that there is still a large gap to be filled. It is well, however, to have such an authoritative and dependable compilation.

**Growth and Development of the Child: Part II. Anatomy and Physiology.**

Report of the Committee on Growth and Development, White House Conference on Child Health and Protection. Kenneth D. Blackfan, M.D., Chairman. Price, \$4. Pp. 629. New York: Century Company, 1933.

Previous publications resulting from the White House Conference on Child Health and Protection have been reviewed. The second in a series of four volumes dealing with the question of growth and development concerns itself with the anatomy and physiology of the whole body. The authors are leaders in their respective branches, and this fact bespeaks the scientific thoroughness with which the book is written.

The nervous system is dealt with as follows: the general development; the histogenesis of the cerebral cortex; cranial topography in childhood; the spinal cord; myelination of the nerve fibers and their functions; the development of reflex behavior; the development of the centers in the spinal cord and the brain; the nerve centers; the visual mechanism; the internal and the middle ear, and the glands of internal secretion.

All of the book is of interest. It is not, however, intended for the layman; it is too technical. This is to some extent regrettable, for many laymen will buy the series. The book is intended as a guide for the two volumes that follow, first, "Interpretation," and second, "Appraisal of the Child." The latter consists of a study of the child as an individual and of the factors that contribute to his mental and physical differences, as an individual.

**Clinique et thérapeutique hydro-climatique.** By Maurice Villaret and L. Justin-Besançon. Price, 30 francs. Pp. 252. Paris: Masson & Cie, 1932.

This is an excellent monograph on hydroclimatology as confined exclusively to France. It contains an introductory historical chapter which, however, does not pretend to enumerate and describe all the mineral springs for hydrotherapeutic practice through the centuries. The distinguishing feature of the book is the exposition of the nature of the various diseases considered and the rationale of the various spas recommended for their mineral and climatic healing virtues.

While emphasizing the undisputed value of crenotherapy by sulphur-laden waters in conjunction with the administration of mercurials and bismuth, a distinction is dogmatically made between the therapeutic indications for each mineral water in relation to the different manifestations of syphilis. For the specific treatment of neurosyphilis, and especially tabes, as well as painful neuritis, hemiplegic sequelae and myelitis, the station at Lamalou is recommended. In cases in which pain is severe, the station at Neris is equally indicated.

**Anatomie des Menschen.** By Hermann Braus. Volume III. Centrales Nervensystem, von Curt Elze. Price, 14.80 marks. Pp. 234. Berlin: Julius Springer, 1932.

The third volume on the anatomy of man is devoted to the central nervous system. Hermann Braus, who died in 1924, was the author of the first two volumes.

The present volume was begun by Professor Braus, and when Elze took it over for completion there was only a bare skeleton; he never had the opportunity of discussing its plan of presentation with the original author. The book therefore is really by Elze.

The presentation of the material follows the usual plan; that is, there is first a discussion of the morphology and development of the nervous system, with comments on the neuron theory, degeneration and the neuroglia. This is followed by the presentation of the spinal cord, cerebrum, cerebellum, meninges and vessels. The subject is adequately covered. There are some excellent illustrations, and the color work is good. It is adequate for students.

**The Practical Medicine Series of Year Books. Neurology.** Edited by Peter Bassoe, M.D. **Psychiatry.** Edited by Franklin G. Ebaugh, A.B., M.D. Series, 1932. Price, \$2.25. Pp. 488. Chicago: Year Book Publishers, Inc., 1933.

The Practical Medicine Series Year Book on Neurology and Psychiatry, edited by Peter Bassoe and Franklin G. Ebaugh, is as usual well done. It is of interest that the neurologic editor considers the outstanding contribution of the year Cushing's description of the clinical picture of basophilic adenoma of the hypophysis. Second in importance he places Cushing's contribution to the relationship between lesions of the brain and gastric ulcer. The psychiatric editor does not mention any outstanding contributions. However, he notes with pleasure that in the preceding year "there is less of an element of propaganda than previously. The literature for the past year also indicates the lack of well organized research in the psychiatric field." No further comment on the progress in these two fields is necessary.

**Krankheitserreger und Gewebefund bei multipler Sklerose: Vergleichend-histologisch-parasitologische Untersuchungen bei multipler Sklerose und anderen Spirochätosen.** By Prof. Gabriel Steiner, Heidelberg. Price, 24 marks. Pp. 196, with 71 illustrations. Berlin: Julius Springer, 1931.

This book is divided into three large, general divisions. The first has to do with the new methods of investigation of spirochetes in the tissues of man and animals; the second concerns the problem of dementia paralytica; the third discusses the application of these new methods to the problem of the etiology of multiple sclerosis. Steiner has written a careful analysis of the problem of the cause of multiple sclerosis. He has considered this problem from many points of view, and he is conservative in his conclusions in that he observes that further proof is required to state finally and certainly that the cause of multiple sclerosis is *Spirochaeta myelophthora*. The illustrations are excellent, and the bibliography is full.

**Les séquelles de l'encéphalite épidémique.** By Georges Guillain and Pierre Mollaret. Price, 28 francs. Pp. 104. Paris: Gaston Doin & Cie, 1932.

This monograph is one of a series of books written for the general practitioner on specific medical topics. It is really a recitation of the various manifestations and syndromes of this protean disease. The numerous motor, sensory, vegetative and psychic symptoms are described briefly, with frequent reference to the literature. Therapy is merely touched on; pathology not at all.

## News and Comment

### GRADUATE CONGRESS IN NEUROLOGY AND PSYCHIATRY

Graduate courses in neurology and psychiatry are offered by Columbia University College of Physicians and Surgeons and cooperating institutes, beginning Oct. 2, 1933. These courses are designed for graduate medical students. In addition to the clinical survey they aim to cover, in part, the sociologic and educational fields. They are so arranged as to meet the desire of applicants feeling the need of further knowledge in these branches. Among the sources of clinical material are the psychiatric and neurologic outpatient departments of the Vanderbilt Clinic, the Montefiore Hospital, the Psychiatric Institute and Hospital and the Neurological Institute of New York. The courses consist of lectures, lectures with laboratory work, lectures with demonstrations, laboratory courses, demonstrations and practical clinical courses.

During the first ten weeks of the academic year beginning Oct. 2, 1933, and ending Dec. 8, 1933, there will be a series of courses devoted principally to clinical psychiatry and neurology. Any individual course (except clinical assignments in neurology and psychiatry) may be taken singly. The sixteen weeks beginning Jan. 22, 1934, and ending May 12, 1934 (semester in neuropathology), are devoted entirely to intensive work in neuropathology, the object being to give a fundamental training in this subject. This work is largely under the supervision of the department of neuropathology of the Psychiatric Institute and Hospital.

The various conferences scheduled are open to those taking any of the courses without payment of additional fees. The entire trimester in neurology and psychiatry may be taken for a fee of \$200. The total fee for the semester in neuropathology is \$250, although the lectures in this semester may be taken separately for a fee of \$100, thus omitting the laboratory practice.

All applicants for admission must receive the approval of the dean of the School of Medicine or his representative. A blank form of application of admission will be furnished by Dr. Howard W. Potter, Psychiatric Institute, 722 West 168th Street, New York City, to whom all communications concerning the course should be addressed.

### PRIZE CONTEST FOR RESEARCH ON THE GENETICS OF MENTAL DISORDERS

The Eugenics Research Association offers a first prize of \$3,000 and a second prize of \$1,000 for original researches on the "Probability of Commitment for a Mental Disorder of Any Kind, Based on the Individual Family History." The probability of commitment to an institution is the criterion on which the research must hinge, but contestants are at liberty to pursue without prejudice their own technic in making investigations.

The association will consider it an advantage to be notified by those who have the intention to enter the contest, and the secretary will be glad to answer any inquiries in regard to it. It is not obligatory, however, on a contestant to notify the association of his purpose before presenting his report. Two years will be allowed for making and completing the studies. Typewritten reports are to be presented to the Eugenics Research Association on or before July 1, 1935, under a nom-de-plume, accompanied by a sealed envelop containing the name and address of the contestant. The awards will then be made by three judges appointed by the association, whose decision shall be final. The text of the prize-winning researches will be published in book form by the Eugenics Research Association.

Further information and suggestions can be secured by writing to the Contest Committee, Eugenics Research Association, Cold Spring Harbor, Long Island, N. Y.